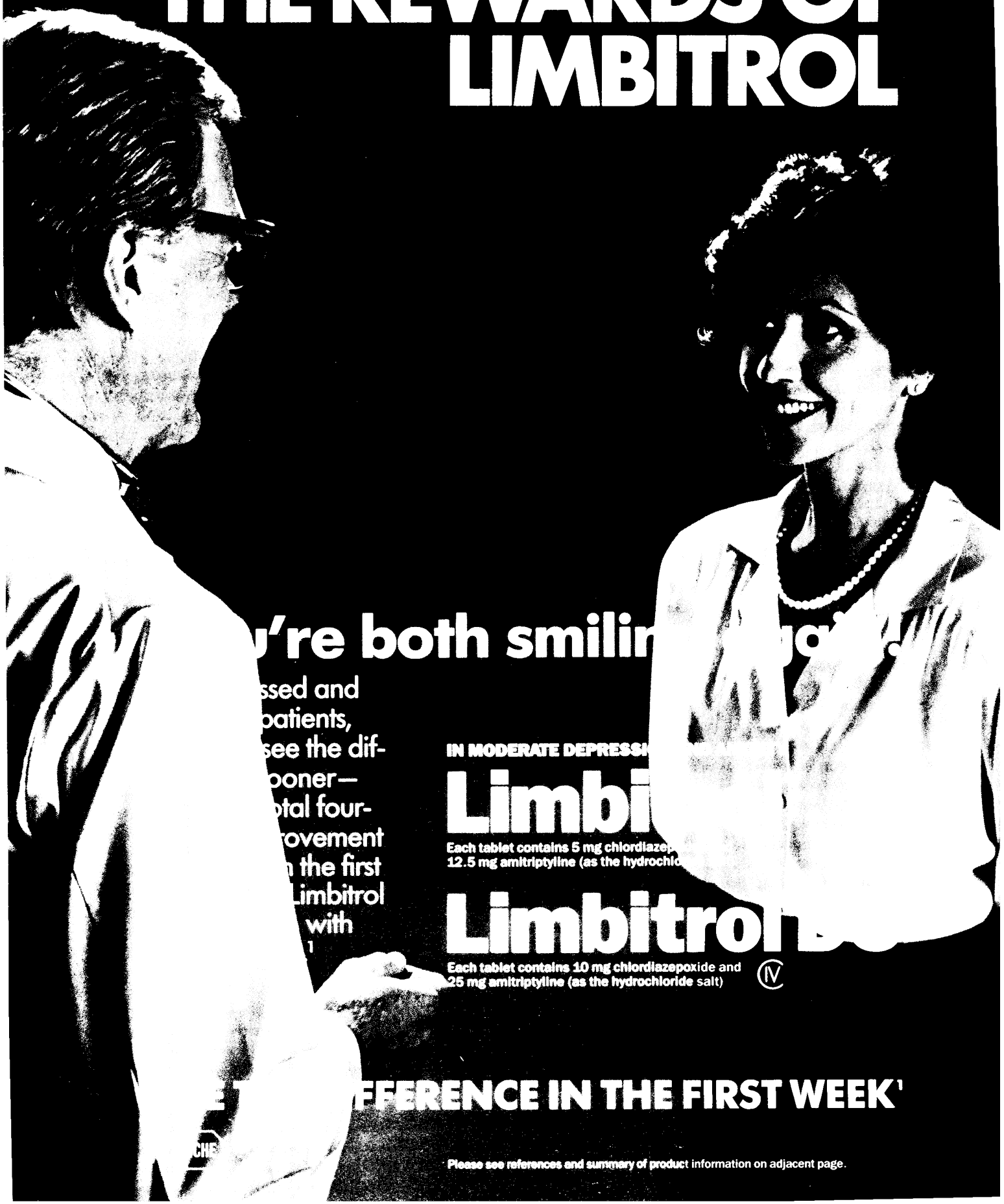
THE REWARDS OF LIMBITROL



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Each tablet contains 5 mg chlordiaze...
12.5 mg amitriptyline (as the hydrochlo...

Limbitro...

Each tablet contains 10 mg chlordiazepoxide and
25 mg amitriptyline (as the hydrochloride salt) (IV)

...FFERENCE IN THE FIRST WEEK[1]

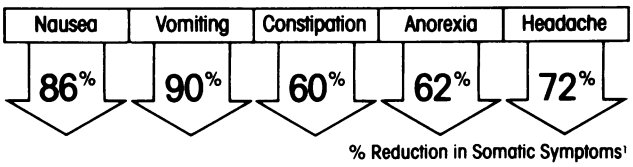
...CHE...

Please see references and summary of product information on adjacent page.

See the difference in the first week[1]

Significantly faster relief—62% of total four-week improvement evident in first week versus 44% with amitriptyline alone[1]

Dramatic first-week reduction in somatic complaints[2]



% Reduction in Somatic Symptoms[1]

Only ⅓ the dropout rate due to side effects of amitriptyline alone, although the incidence of side effects is similar[1]

Caution patients about the combined effects of Limbitrol with alcohol or other CNS depressants and about activities requiring complete mental alertness, such as operating machinery or driving a car. In general, limit dosage to the lowest effective amount in elderly patients.

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Protect your decision. Write "Do not substitute."

Limbitrol®

Each tablet contains 5 mg chlordiazepoxide and 12.5 mg amitriptyline (as the hydrochloride salt) Ⓝ

Limbitrol® DS

Each tablet contains 10 mg chlordiazepoxide and 25 mg amitriptyline (as the hydrochloride salt) Ⓝ

References: 1. Feighner JP, *et al: Psychopharmacology 61*:217-225, Mar 22, 1979. **2.** Data on file, Hoffmann-La Roche Inc., Nutley, NJ.

Limbitrol® Ⓝ
Tranquilizer—Antidepressant
Before prescribing, please consult complete product information, a summary of which follows:
Indications: Relief of moderate to severe depression associated with moderate to severe anxiety.
Contraindications: Known hypersensitivity to benzodiazepines or tricyclic antidepressants. Do not use with monoamine oxidase (MAO) inhibitors or within 14 days following discontinuation of MAO inhibitors since hyperpyretic crises, severe convulsions and deaths have occurred with concomitant use; then initiate cautiously, gradually increasing dosage until optimal response is achieved. Contraindicated during acute recovery phase following myocardial infarction.
Warnings: Use with great care in patients with history of urinary retention or angle-closure glaucoma. Severe constipation may occur in patients taking tricyclic antidepressants and anticholinergic-type drugs. Closely supervise cardiovascular patients. (Arrhythmias, sinus tachycardia and prolongation of conduction time reported with use of tricyclic antidepressants, especially high doses. Myocardial infarction and stroke reported with use of this class of drugs.) Caution patients about possible combined effects with alcohol and other CNS depressants and against hazardous occupations requiring complete mental alertness (*e.g.*, operating machinery, driving).

***Usage in Pregnancy:* Use of minor tranquilizers during the first trimester should almost always be avoided because of increased risk of congenital malformations as suggested in several studies. Consider possibility of pregnancy when instituting therapy; advise patients to discuss therapy if they intend to or do become pregnant.**

Since physical and psychological dependence to chlordiazepoxide have been reported rarely, use caution in administering Limbitrol to addiction-prone individuals or those who might increase dosage; withdrawal symptoms following discontinuation of either component alone have been reported (nausea, headache and malaise for amitriptyline; symptoms [including convulsions] similar to those of barbiturate withdrawal for chlordiazepoxide).
Precautions: Use with caution in patients with a history of seizures, in hyperthyroid patients or those on thyroid medication, and in patients with impaired renal or hepatic function. Because of the possibility of suicide in depressed patients, do not permit easy access to large quantities in these patients. Periodic liver function tests and blood counts are recommended during prolonged treatment. Amitriptyline component may block action of guanethidine or similar antihypertensives. When tricyclic antidepressants are used concomitantly with cimetidine (Tagamet), clinically significant effects have been reported involving delayed elimination and increasing steady state concentrations of the tricyclic drugs. Concomitant use of Limbitrol with other psychotropic drugs has not been evaluated; sedative effects may be additive. Discontinue several days before surgery. Limit concomitant administration of ECT to essential treatment. See Warnings for precautions about pregnancy. Limbitrol should not be taken during the nursing period. Not recommended in children under 12. In the elderly and debilitated, limit to smallest effective dosage to preclude ataxia, oversedation, confusion or anticholinergic effects.
Adverse Reactions: Most frequently reported are those associated with either component alone: drowsiness, dry mouth, constipation, blurred vision, dizziness and bloating. Less frequently occurring reactions include vivid dreams, impotence, tremor, confusion and nasal congestion. Many depressive symptoms including anorexia, fatigue, weakness, restlessness and lethargy have been reported as side effects of both Limbitrol and amitriptyline. Granulocytopenia, jaundice and hepatic dysfunction have been observed rarely.
The following list includes adverse reactions not reported with Limbitrol but requiring consideration because they have been reported with one or both components or closely related drugs:
Cardiovascular: Hypotension, hypertension, tachycardia, palpitations, myocardial infarction, arrhythmias, heart block, stroke.
Psychiatric: Euphoria, apprehension, poor concentration, delusions, hallucinations, hypomania and increased or decreased libido.
Neurologic: Incoordination, ataxia, numbness, tingling and paresthesias of the extremities, extrapyramidal symptoms, syncope, changes in EEG patterns.
Anticholinergic: Disturbance of accommodation, paralytic ileus, urinary retention, dilatation of urinary tract.
Allergic: Skin rash, urticaria, photosensitization, edema of face and tongue, pruritus.
Hematologic: Bone marrow depression including agranulocytosis, eosinophilia, purpura, thrombocytopenia.
Gastrointestinal: Nausea, epigastric distress, vomiting, anorexia, stomatitis, peculiar taste, diarrhea, black tongue.
Endocrine: Testicular swelling and gynecomastia in the male, breast enlargement, galactorrhea and minor menstrual irregularities in the female, elevation and lowering of blood sugar levels, and syndrome of inappropriate ADH (antidiuretic hormone) secretion.
Other: Headache, weight gain or loss, increased perspiration, urinary frequency, mydriasis, jaundice, alopecia, parotid swelling.
Overdosage: Immediately hospitalize patient suspected of having taken an overdose. Treatment is symptomatic and supportive. I.V. administration of 1 to 3 mg physostigmine salicylate has been reported to reverse the symptoms of amitriptyline poisoning. See complete product information for manifestation and treatment.
Dosage: Individualize according to symptom severity and patient response. Reduce to smallest effective dosage when satisfactory response is obtained. Larger portion of daily dose may be taken at bedtime. Single *h.s.* dose may suffice for some patients. Lower dosages are recommended for the elderly. Limbitrol DS (double strength) Tablets, initial dosage of three or four tablets daily in divided doses, increased up to six tablets or decreased to two tablets daily as required. Limbitrol Tablets, initial dosage of three or four tablets daily in divided doses, for patients who do not tolerate higher doses.
How Supplied: *Double strength (DS) Tablets,* white, film-coated, each containing 10 mg chlordiazepoxide and 25 mg amitriptyline (as the hydrochloride salt), and *Tablets,* blue, film-coated, each containing 5 mg chlordiazepoxide and 12.5 mg amitriptyline (as the hydrochloride salt). Available in bottles of 100 and 500; Tel-E-Dose® packages of 100; Prescription Paks of 50.

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For more than ten years, we've provided the highest quality protection for substantially lower cost. How did we do it? Two important factors are: careful selection of our members and physician involvement in loss prevention and education. More than 42% of our members have incurred less than $2,500 in claims expenses over the past five year period. When you join us, you'll be joining peers who have a long-term track record of overall low risk. That keeps all of our members' costs down. Including yours.

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	Southern California			Northern California		
Specialty	Composite* Insurance Companies	CAP/MPT	Savings with CAP/MPT	Composite* Insurance Companies	CAP/MPT	Savings with CAP/MPT
Psychiatry	$ 5,100	$ 2,365	54%	$ 3,789	$ 2,052	46%
Pediatrics	7,358	2,365	68%	6,208	2,052	67%
Urology	18,571	13,735	26%	14,560	11,776	19%
Anesthesiology	20,113	13,735	32%	16,621	11,776	29%
General Surgery	30,838	17,853	42%	22,388	15,306	32%
Plastic Surgery	31,554	17,853	43%	22,961	15,306	33%
Orthopedic Surgery w/Spinal	39,744	21,971	45%	34,184	18,837	45%
Obstetrics/ Gynecology	49,696	21,971	56%	40,220	18,837	53%

*Insurance company composite rates are averages based upon 4/1/87 rates of The Doctors' Company, 6/1/87 rates of MIEC, 1988 rates of Norcal and SCPIE. Details of source data on request. No costs shown here for San Diego or Imperial County. Other surcharges, credits, reductions may apply. All costs based on mature rate (including retroactive coverage).

CAP/MPT costs are based on dues and January 1988 mature assessments. They do not include the $200 membership fee and refundable initial trust contribution amounts.

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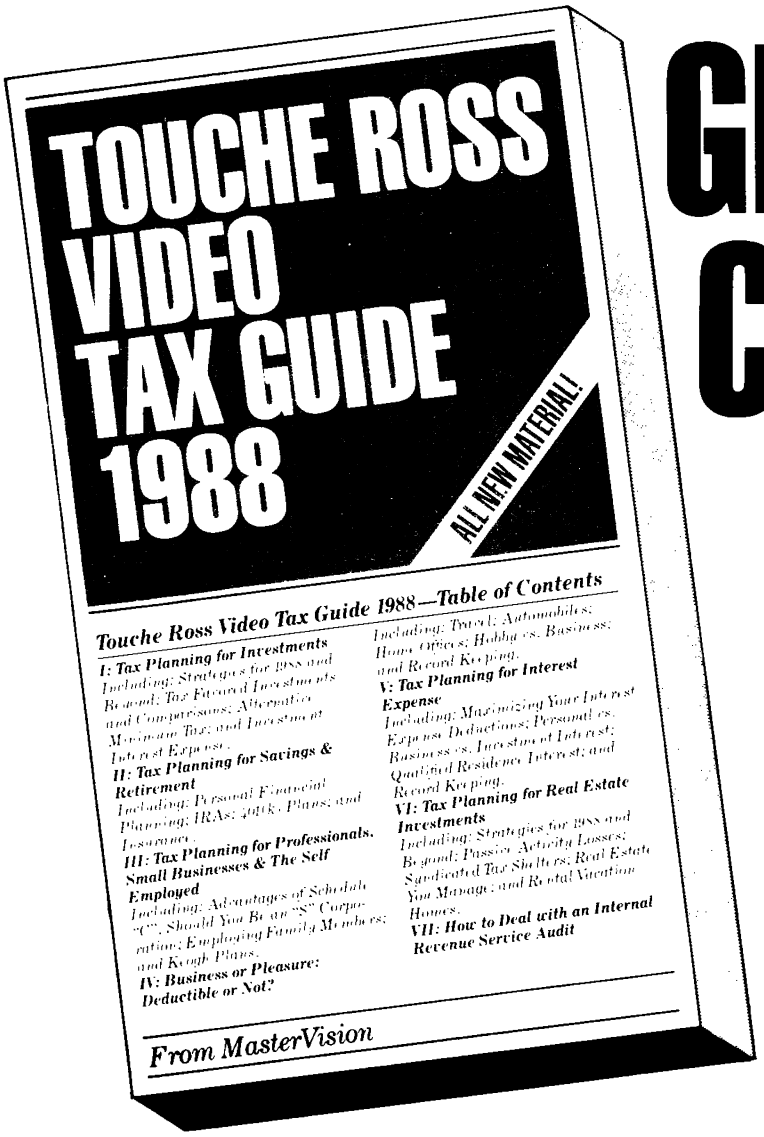

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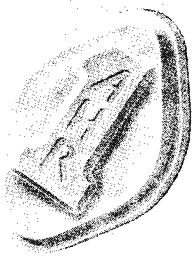

TENEX®

(Guanfacine HCl)

A·H·ROBINS Pharmaceutical Division, Richmond, Virginia 23261-6609
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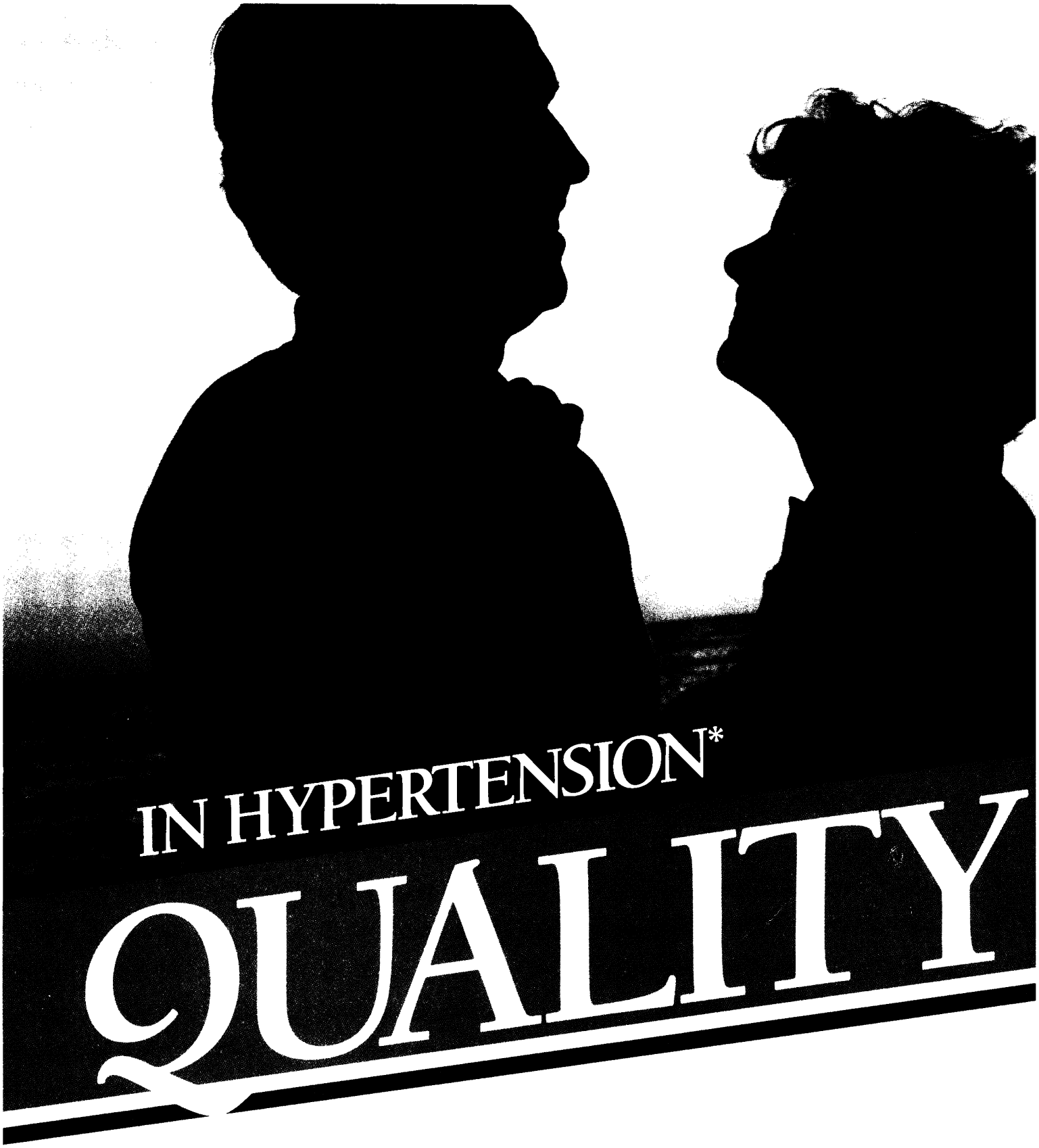


***CAPOTEN® (captopril tablets) may be used as initial therapy only for patients with normal renal function in whom the risk of neutropenia/agranulocytosis is relatively low (1 out of over 8,600 in clinical trials). Use special precautions in patients with impaired renal function, collagen vascular disorders, or those exposed to other drugs known to affect the white cells or immune response. Evaluation of hypertensives should always include assessment of renal function. Overall, the most frequently occurring adverse reactions associated with CAPOTEN are skin rash and taste alteration; both effects are generally mild, reversible, or self-limited. See INDICATIONS AND USAGE, WARNINGS, and ADVERSE REACTIONS in the brief summary on the adjacent page.**

†Based upon the Sexual Symptoms Distress Index.

1. Croog SH, Levine S, Testa MA, et al: The effects of antihypertensive therapy on the quality of life. N Engl J Med 314(26):1657-1664, 1986.

SQUIBB

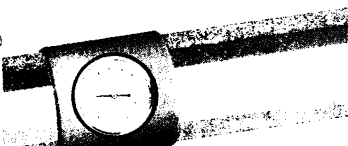
Means Sharing Love

Staying close can be important to your hypertensive patients. Unfortunately, this aspect of patients' lives can be complicated by drug-induced effects upon sexual function.

CAPOTEN has been shown to maintain sexual interest and function.†[1] It's one of many good reasons to choose CAPOTEN for blood pressure control...that helps maintain patients' quality of life.

These data are based on a multicenter, randomized, 24-week study of 626 mild-to-moderate hypertensive male patients with normal renal function, 181 of whom received captopril.

OF LIFE



THE CAPOTEN® (captopril tablets) DIFFERENCE

QUALITY OF LIFE THE CAPOTEN® (captopril tablets) DIFFERENCE

CAPOTEN® TABLETS

Captopril Tablets

INDICATIONS: Hypertension – CAPOTEN (captopril) is indicated for the treatment of hypertension. Consideration should be given to the risk of neutropenia/agranulocytosis (see WARNINGS). CAPOTEN may be used as initial therapy for patients with normal renal function, in whom the risk is relatively low. In patients with impaired renal function, particularly those with collagen vascular disease, captopril should be reserved for those who have either developed unacceptable side effects on other drugs, or have failed to respond satisfactorily to drug combinations. CAPOTEN is effective alone and in combination with other antihypertensive agents, especially thiazide-type diuretics.

Heart Failure: CAPOTEN (captopril) is indicated in patients with heart failure who have not responded adequately to or cannot be controlled by conventional diuretic and digitalis therapy. CAPOTEN is to be used with diuretics and digitalis.

CONTRAINDICATIONS: CAPOTEN is contraindicated in patients who are hypersensitive to this product.

WARNINGS: Neutropenia/Agranulocytosis – Neutropenia ($< 1000/mm^3$) with myeloid hypoplasia has resulted from use of captopril. About half of the neutropenic patients developed systemic or oral cavity infections or other features of the syndrome of agranulocytosis. The risk of neutropenia is dependent on the clinical status of the patient:

In clinical trials in patients with hypertension who have normal renal function (serum creatinine less than 1.6 mg/dL and no collagen vascular disease), neutropenia has been seen in one patient out of over 8,600 exposed. In patients with some degree of renal failure (serum creatinine at least 1.6 mg/dL) but no collagen vascular disease, the risk in clinical trials was about 1 per 500. Doses were relatively high in these patients, particularly in view of their diminished renal function. In patients with collagen vascular diseases (e.g., systemic lupus erythematosus, scleroderma) and impaired renal function, neutropenia occurred in 3.7% of patients in clinical trials. While none of the over 750 patients in formal clinical trials of heart failure developed neutropenia, it has occurred during the subsequent clinical experience. Of reported cases, about half had serum creatinine ≥ 1.6 mg/dL and more than 75% received procainamide. In heart failure, it appears that the same risk factors for neutropenia are present.

Neutropenia has appeared usually within 3 months after starting therapy, associated with myeloid hypoplasia and frequently accompanied by erythroid hypoplasia and decreased numbers of megakaryocytes (e.g., hypoplastic bone marrow and pancytopenia); anemia and thrombocytopenia were sometimes seen. Neutrophils generally returned to normal in about 2 weeks after captopril was discontinued, and serious infections were limited to clinically complex patients. About 13% of the cases of neutropenia have ended fatally, but almost all fatalities were in patients with serious illness, having collagen vascular disease, renal failure, heart failure or immunosuppressant therapy, or a combination of these complicating factors. **Evaluation of the hypertensive or heart failure patient should always include assessment of renal function.** If captopril is used in patients with impaired renal function, white blood cell and differential counts should be evaluated prior to starting treatment and at approximately 2-week intervals for about 3 months, then periodically. In patients with collagen vascular disease or who are exposed to other drugs known to affect the white cells or immune response, particularly when there is impaired renal function, captopril should be used only after an assessment of benefit and risk, and then with caution. All patients treated with captopril should be told to report any signs of infection (e.g., sore throat, fever). If infection is suspected, perform white cell counts without delay. Since discontinuation of captopril and other drugs has generally led to prompt return of the white count to normal, upon confirmation of neutropenia (neutrophil count $< 1000/mm^3$) withdraw captopril and closely follow the patient's course.

Proteinuria: Total urinary proteins >1 g per day were seen in about 0.7% of patients on captopril. About 90% of affected patients had evidence of prior renal disease or received high doses (>150 mg/day), or both. The nephrotic syndrome occurred in about one-fifth of proteinuric patients. In most cases, proteinuria subsided or cleared within 6 months whether or not captopril was continued. The BUN and creatinine were seldom altered in proteinuric patients. Since most cases of proteinuria occurred by the 8th month of therapy with captopril, patients with prior renal disease or those receiving captopril at doses >150 mg per day, should have urinary protein estimates (dip-stick on 1st morning urine) before therapy, and periodically thereafter.

Hypotension: Excessive hypotension was rarely seen in hypertensive patients but is a possibility in severely salt/volume-depleted persons such as those treated vigorously with diuretics (see PRECAUTIONS [Drug Interactions]). In heart failure, where the blood pressure was either normal or low, transient decreases in mean blood pressure ~20% were recorded in about half of the patients. This transient hypotension may occur after any of the first several doses and is usually well tolerated, although rarely it has been associated with arrhythmia or conduction defects. A starting dose of 6.25 or 12.5 mg tid may minimize the hypotensive effect. Patients should be followed closely for the first 2 weeks of treatment and whenever the dose of captopril and/or diuretic is increased.

BECAUSE OF THE POTENTIAL FALL IN BLOOD PRESSURE IN THESE PATIENTS, THERAPY SHOULD BE STARTED UNDER VERY CLOSE MEDICAL SUPERVISION.

PRECAUTIONS: General: *Impaired Renal Function* – Hypertension – Some hypertensive patients with renal disease, particularly those with severe renal artery stenosis, have developed increases in BUN and serum creatinine. It may be necessary to reduce captopril dosage and/or discontinue diuretic. For some of these patients, normalization of blood pressure and maintenance of adequate renal perfusion may not be possible. Heart Failure – About 20% of patients develop stable elevations of BUN and serum creatinine >20% above normal or baseline upon long-term treatment. Less than 5% of patients, generally with severe preexisting renal disease, required discontinuation due to progressively increasing creatinine. See DOSAGE AND ADMINISTRATION, ADVERSE REACTIONS [Altered Laboratory Findings]. *Valvular Stenosis* – A theoretical concern, for risk of decreased coronary perfusion, has been noted regarding vasodilator treatment in patients with aortic stenosis due to decreased afterload reduction. *Surgery/Anesthesia* – If hypotension occurs during surgery or anesthesia, and is considered due to the effects of captopril, it is correctable by volume expansion.

Drug Interactions: *Hypotension – Patients on Diuretic Therapy* – Precipitous reduction of blood pressure may occasionally occur within the 1st hour after administration of the initial of captopril dose in patients on diuretics, especially those recently placed on diuretics, and those on severe dietary salt restriction or dialysis. This possibility can be minimized by either discontinuing the diuretic or increasing the salt intake about 1 week prior to initiation of captopril therapy or by initiating therapy with small doses (6.25 or 12.5 mg). Alternatively, provide medical supervision for at least 1 hour after the initial dose.

Agents Having Vasodilator Activity – In heart failure patients, vasodilators should be administered with caution.

Agents Causing Renin Release – Captopril's effect will be augmented by antihypertensive agents that cause renin release.

Agents Affecting Sympathetic Activity – The sympathetic nervous system may be especially important in supporting blood pressure in patients receiving captopril alone or with diuretics. Beta-adrenergic blocking drugs add some further antihypertensive effect to captopril, but the overall response is less than additive. Therefore, use agents affecting sympathetic activity (e.g., ganglionic blocking agents or adrenergic neuron blocking agents) with caution.

Agents Increasing Serum Potassium – Give potassium-sparing diuretics or potassium supplements only for documented hypokalemia, and then with caution, since they may lead to a significant increase of serum potassium. Use potassium-containing salt substitutes with caution.

Inhibitors of Endogenous Prostaglandin Synthesis – Indomethacin and other nonsteroidal anti-inflammatory agents may reduce the antihypertensive effect of captopril, especially in low renin hypertension.

Drug/Laboratory Test Interaction: Captopril may cause a false-positive urine test for acetone.

Carcinogenesis, Mutagenesis and Impairment of Fertility: Two-year studies with doses of 50 to 1350 mg/kg/day in mice and rats failed to show any evidence of carcinogenic potential. Studies in rats have revealed no impairment of fertility.

Pregnancy: Category C: There are no adequate and well-controlled studies in pregnant women. Embryocidal effects and craniofacial malformations were observed in rabbits. Therefore, captopril should be used during pregnancy, or for patients likely to become pregnant, only if the potential benefit outweighs the potential risk to the fetus. Captopril crosses the human placenta.

Nursing Mothers: Captopril is secreted in human milk. Exercise caution when administering captopril to a nursing woman, and, in general, nursing should be interrupted.

Pediatric Use: Safety and effectiveness in children have not been established although there is limited experience with use of captopril in children from 2 months to 15 years of age. Dosage, on a weight basis, was comparable to that used in adults. CAPOTEN (captopril) should be used in children only if other measures for controlling blood pressure have not been effective.

ADVERSE REACTIONS: Reported incidences are based on clinical trials involving approximately 7000 patients.

Renal – About 1 of 100 patients developed proteinuria (see WARNINGS). Renal insufficiency, renal failure, polyuria, oliguria, and urinary frequency in 1 to 2 of 1000 patients.

Hematologic – Neutropenia/agranulocytosis has occurred (see WARNINGS). Anemia, thrombocytopenia, and pancytopenia have been reported.

Dermatologic – Rash, (usually maculopapular, rarely urticarial), often with pruritus, and sometimes with fever and eosinophilia, in about 4 to 7 of 100 patients (depending on renal status and dose), usually during the 1st 4 weeks of therapy. Pruritus, without rash, in about 2 of 100 patients. A reversible associated pemphigoid-like lesion, and photosensitivity, have also been reported. Angioedema of the face, mucous membranes of the mouth, or of the extremities in about 1 of 1000 patients – reversible on discontinuance of captopril therapy. One case of laryngeal edema has been reported. Flushing or pallor in 2 to 5 of 1000 patients.

Cardiovascular – Hypotension may occur; see WARNINGS and PRECAUTIONS [Drug Interactions] for discussion of hypotension on initiation of captopril therapy. Tachycardia, chest pain, and palpitations each in about 1 of 100 patients. Angina pectoris, myocardial infarction, Raynaud's syndrome, and congestive heart failure each in 2 to 3 of 1000 patients.

Dysgeusia – Approximately 2 to 4 (depending on renal status and dose) of 100 patients developed a diminution or loss of taste perception; taste impairment is reversible and usually self-limited even with continued drug use (2 to 3 months). Gastric irritation, abdominal pain, nausea, vomiting, diarrhea, anorexia, constipation, aphthous ulcers, peptic ulcer, dizziness, headache, malaise, fatigue, insomnia, dry mouth, dyspnea, cough, alopecia, paresthesias reported in about 0.5 to 2% of patients but did not appear at increased frequency compared to placebo or other treatments used in controlled trials.

Altered Laboratory Findings: Elevations of liver enzymes in a few patients although no causal relationship has been established. Rarely cholestatic jaundice, and hepatocellular injury with or without secondary cholestasis, have been reported. A transient elevation of BUN and serum creatinine may occur, especially in volume-depleted or renovascular hypertension patients. In instances of rapid reduction of longstanding or severely elevated blood pressure, the glomerular filtration rate may decrease transiently, also resulting in transient rises in serum creatinine and BUN. Small increases in serum potassium concentration frequently occur, especially in patients with renal impairment (see PRECAUTIONS).

OVERDOSAGE: Primary concern is correction of hypotension. Volume expansion with an I.V. infusion of normal saline is the treatment of choice for restoration of blood pressure. Captopril may be removed from the general circulation by hemodialysis.

DOSAGE AND ADMINISTRATION: CAPOTEN (captopril) should be taken one hour before meals. In hypertension, CAPOTEN may be dosed bid or tid. Dosage must be individualized; see DOSAGE AND ADMINISTRATION section of package insert for detailed information regarding dosage in hypertension and in heart failure. Because CAPOTEN (captopril) is excreted primarily by the kidneys, dosage adjustments are recommended for patients with impaired renal function.

Consult package insert before prescribing CAPOTEN (captopril).

HOW SUPPLIED: Available in tablets of 12.5, 25, 50, and 100 mg in bottles of 100 (25 mg and 50 mg also available in bottles of 1000), and in UNIMATIC® unit-dose packs of 100 tablets. (J3-658J)

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527-593 Issued: January 1988

The World's Most Popular K*

Slow-K®

potassium chloride
slow-release tablets
8 mEq (600 mg)

It means "dependability" in almost any language

*Based on worldwide sales data on file, CIBA Pharmaceutical Company.

Capsule or tablet slow-release potassium chloride preparations should be reserved for patients who cannot tolerate, refuse to take, or have compliance problems with liquid or effervescent potassium preparations because of reports of intestinal and gastric ulceration and bleeding with slow-release KCl preparations.

Before prescribing, please consult Brief Prescribing Information on next page.

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CIBA

128-3568-A

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For good reasons

- ☐ **It works**—a 12-year record of efficacy[1]
- ☐ **It's safe**—unsurpassed by any other KCl tablet or capsule[2]*
- ☐ **It's acceptable vs liquids**—greater palatability, fewer GI complaints, lower incidence of nausea[2]
- ☐ **It's comparable to 10 mEq**—in low-dosage supplementation[3†]
- ☐ **It's economical**—less expensive than all other leading KCl slow-release supplements on a per tablet cost to the patient[1]

Slow-K®
potassium chloride
slow-release tablets 8 mEq (600 mg)

For patients who can't or won't tolerate liquid KCl.

*The most common adverse reactions to potassium salts are gastrointestinal side effects.

†Pooled mean serum potassium following oral administration of 30 mEq K-Tab compared to 24 mEq Slow-K in diuretic-treated hypertensives (n = 20) over 8 weeks.

C I B A

References: 1. Data on file, CIBA Pharmaceutical Company. **2.** Skoutakis VA, Acchiardo SR, Wojciechowski NJ, et al: Liquid and solid potassium chloride: Bioavailability and safety. *Pharmacotherapy* 1980;4(6):392-397. **3.** Skoutakis VA, Carter CA, Acchiardo SR: Therapeutic assessment of Slow-K and K-Tab potassium chloride formulations in hypertensive patients treated with thiazide diuretics. *Drug Intell Clin Pharm* 1987;21:436-440.

Slow-K®
potassium chloride USP
Slow-Release Tablets
8 mEq (600 mg)

BRIEF SUMMARY (FOR FULL PRESCRIBING INFORMATION SEE PACKAGE INSERT)

INDICATIONS AND USAGE
BECAUSE OF REPORTS OF INTESTINAL AND GASTRIC ULCERATION AND BLEEDING WITH SLOW-RELEASE POTASSIUM CHLORIDE PREPARATIONS, THESE DRUGS SHOULD BE RESERVED FOR THOSE PATIENTS WHO CANNOT TOLERATE OR REFUSE TO TAKE LIQUID OR EFFERVESCENT POTASSIUM PREPARATIONS OR FOR PATIENTS IN WHOM THERE IS A PROBLEM OF COMPLIANCE WITH THESE PREPARATIONS.
1. For therapeutic use in patients with hypokalemia with or without metabolic alkalosis; in digitalis intoxication and in patients with hypokalemic familial periodic paralysis.
2. For prevention of potassium depletion when the dietary intake of potassium is inadequate in the following conditions: patients receiving digitalis and diuretics for congestive heart failure; hepatic cirrhosis with ascites; states of aldosterone excess with normal renal function; potassium-losing nephropathy; and certain diarrheal states.
3. The use of potassium salts in patients receiving diuretics for uncomplicated essential hypertension is often unnecessary when such patients have a normal dietary pattern. Serum potassium should be checked periodically, however, and if hypokalemia occurs, dietary supplementation with potassium-containing foods may be adequate to control milder cases. In more severe cases supplementation with potassium salts may be indicated.

CONTRAINDICATIONS
Potassium supplements are contraindicated in patients with hyperkalemia, since a further increase in serum potassium concentration in such patients can produce cardiac arrest. Hyperkalemia may complicate any of the following conditions: chronic renal failure, systemic acidosis such as diabetic acidosis, acute dehydration, extensive tissue breakdown as in severe burns, adrenal insufficiency, or the administration of a potassium-sparing diuretic (e.g., spironolactone, triamterene) (see OVERDOSAGE).

All solid dosage forms of potassium supplements are contraindicated in any patient in whom there is cause for arrest or delay in tablet passage through the gastrointestinal tract. In these instances, potassium supplementation should be with a liquid preparation. Wax-matrix potassium chloride preparations have produced esophageal ulceration in certain cardiac patients with esophageal compression due to an enlarged left atrium.

WARNINGS
Hyperkalemia (See OVERDOSAGE).
In patients with impaired mechanisms for excreting potassium, the administration of potassium salts can produce hyperkalemia and cardiac arrest. This occurs most commonly in patients given potassium by the intravenous route but may also occur in patients given potassium orally. Potentially fatal hyperkalemia can develop rapidly and be asymptomatic.

The use of potassium salts in patients with chronic renal disease, or any other condition which impairs potassium excretion, requires particularly careful monitoring of the serum potassium concentration and appropriate dosage adjustment.

Interaction With Potassium-Sparing Diuretics
Hypokalemia should not be treated by the concomitant administration of potassium salts and a potassium-sparing diuretic (e.g., spironolactone or triamterene), since the simultaneous administration of these agents can produce severe hyperkalemia.

Gastrointestinal Lesions
Potassium chloride tablets have produced stenotic and/or ulcerative lesions of the small bowel and deaths. These lesions are caused by a high localized concentration of potassium ion in the region of a rapidly dissolving tablet, which injures the bowel wall and thereby produces obstruction, hemorrhage, or perforation. Slow-K is a wax-matrix tablet formulated to provide a controlled rate of release of potassium chloride and thus to minimize the possibility of a high local concentration of potassium ion near the bowel wall. While the reported frequency of small-bowel lesions is much less with wax-matrix tablets (less than one per 100,000 patient-years) than with enteric-coated potassium chloride tablets (40-50 per 100,000 patient-years) cases associated with wax-matrix tablets have been reported both in foreign countries and in the United States. In addition, perhaps because the wax-matrix preparations are not enteric-coated and release potassium in the stomach, there have been reports of upper gastrointestinal bleeding associated with these products. The total number of gastrointestinal lesions remains approximately one per 100,000 patient-years. Slow-K should be discontinued immediately and the possibility of bowel obstruction or perforation considered if severe vomiting, abdominal pain, distention, or gastrointestinal bleeding occurs.

Metabolic Acidosis
Hypokalemia in patients with metabolic *acidosis* should be treated with an alkalinizing potassium salt such as potassium bicarbonate, potassium citrate, or potassium acetate.

PRECAUTIONS
General:
The diagnosis of potassium depletion is ordinarily made by demonstrating hypokalemia in a patient with a clinical history suggesting some cause for potassium depletion. In interpreting the serum potassium level, the physician should bear in mind that acute alkalosis *per se* can produce hypokalemia in the absence of a deficit in total body potassium, while acute acidosis *per se* can increase the serum potassium concentration into the normal range even in the presence of a reduced total body potassium.

Information for Patients
Physicians should consider reminding the patient of the following:
To take each dose without crushing, chewing, or sucking the tablets.
To take this medicine only as directed. This is especially important if the patient is also taking both diuretics and digitalis preparations.
To check with the physician if there is trouble swallowing tablets or if the tablets seem to stick in the throat.
To check with the doctor at once if tarry stools or other evidence of gastrointestinal bleeding is noticed.

Laboratory Tests
Regular serum potassium determinations are recommended. In addition, during the treatment of potassium depletion, careful attention should be paid to acid-base balance, other serum electrolyte levels, the electrocardiogram, and the clinical status of the patient, particularly in the presence of cardiac disease, renal disease, or acidosis.

Drug Interactions
Potassium-sparing diuretics: see WARNINGS.

Carcinogenesis, Mutagenesis, Impairment of Fertility
Long-term carcinogenicity studies in animals have not been performed.

Pregnancy Category C
Animal reproduction studies have not been conducted with Slow-K. It is also not known whether Slow-K can cause fetal harm when administered to a pregnant woman or can affect reproduction capacity. Slow-K should be given to a pregnant woman only if clearly needed.

Nursing Mothers
The normal potassium ion content of human milk is about 13 mEq/L. It is not known if Slow-K has an effect on this content. Caution should be exercised when Slow-K is administered to a nursing woman.

Pediatric Use
Safety and effectiveness in children have not been established.

ADVERSE REACTIONS
One of the most severe adverse effects is hyperkalemia (see CONTRAINDICATIONS, WARNINGS, and OVERDOSAGE). There also have been reports of upper and lower gastrointestinal conditions including obstruction, bleeding, ulceration, and perforation (see CONTRAINDICATIONS and WARNINGS); other factors known to be associated with such conditions were present in many of these patients.

The most common adverse reactions to oral potassium salts are nausea, vomiting, abdominal discomfort, and diarrhea. These symptoms are due to irritation of the gastrointestinal tract and are best managed by taking the dose with meals or reducing the dose.

Skin rash has been reported rarely.

OVERDOSAGE
The administration of oral potassium salts to persons with normal excretory mechanisms for potassium rarely causes serious hyperkalemia. However, if excretory mechanisms are impaired or if potassium is administered too rapidly intravenously, potentially fatal hyperkalemia can result (see CONTRAINDICATIONS and WARNINGS). It is important to recognize that hyperkalemia is usually asymptomatic and may be manifested only by an increased serum potassium concentration (6.5-8.0 mEq/L) and characteristic electrocardiographic changes (peaking of T waves, loss of P wave, depression of S-T segment, and prolongation of the Q-T interval). Late manifestations include muscle paralysis and cardiovascular collapse from cardiac arrest (9-12 mEq/L).

Treatment measures for hyperkalemia include the following: (1) elimination of foods and medications containing potassium and of potassium-sparing diuretics; (2) intravenous administration of 300-500 ml/hr of 10% dextrose solution containing 10-20 units of insulin per 1,000 ml; (3) correction of acidosis, if present, with intravenous sodium bicarbonate; (4) use of exchange resins, hemodialysis, or peritoneal dialysis.

In treating hyperkalemia in patients who have been stabilized on digitalis, too rapid a lowering of the serum potassium concentration can produce digitalis toxicity.

DOSAGE AND ADMINISTRATION
The usual dietary intake of potassium by the average adult is 40-80 mEq per day. Potassium depletion sufficient to cause hypokalemia usually requires the loss of 200 or more mEq of potassium from the total body store. Dosage must be adjusted to the individual needs of each patient but is typically in the range of 20 mEq per day for the prevention of hypokalemia to 40-100 mEq or more per day for the treatment of potassium depletion. Large numbers of tablets should be given in divided doses.

Note: Slow-K slow-release tablets must be swallowed whole and never crushed, chewed, or sucked.

HOW SUPPLIED
Tablets—600 mg of potassium chloride (equivalent to 8 mEq) round, buff colored, sugar-coated (imprinted Slow-K)
Bottles of 100 . . . . . NDC 0083-0165-30
Bottles of 1000 . . . . . NDC 0083-0165-40
Consumer Pack—One Unit
12 Bottles—100 tablets each . . . . . NDC 0083-0165-65
Accu-Pak® Unit Dose (Blister pack)
Box of 100 (strips of 10) . . . . . NDC 0083-0165-32
Do not store above 86°F (30°C). Protect from moisture. Protect from light.

Dispense in tight, light-resistant container (USP).

Dist. by:
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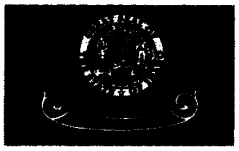

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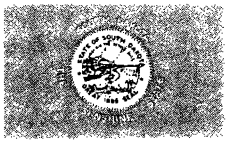

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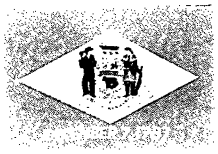

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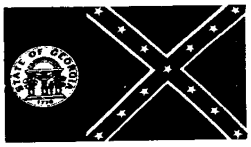

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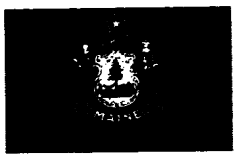

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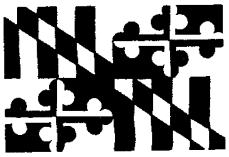

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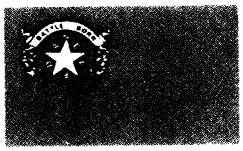

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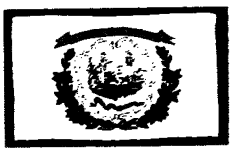

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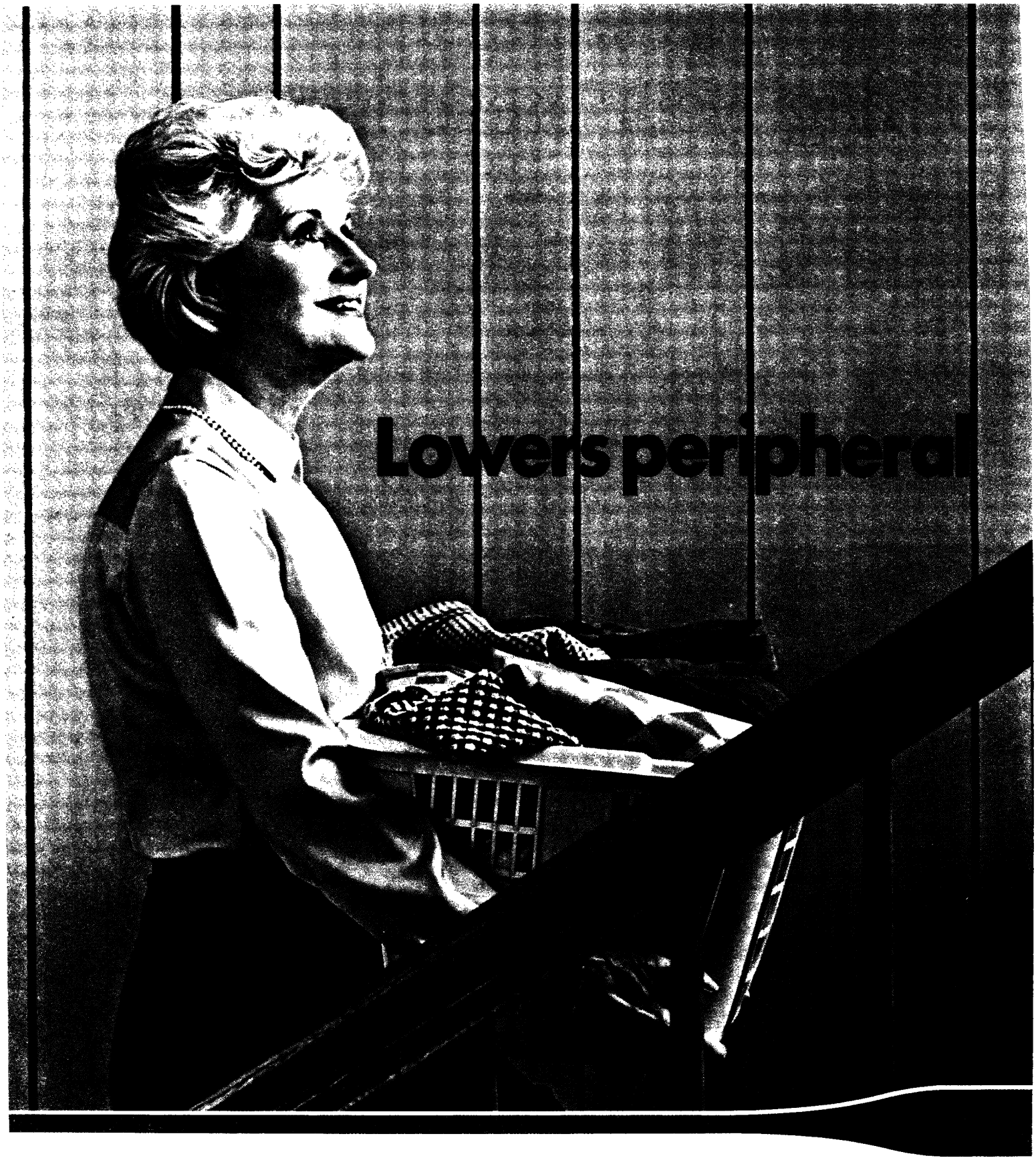

Glaxo

IN HYPERTENSION

resistance in the elderly[1]

- ☐ Effective blood pressure control
- ☐ Low incidence of fatigue,[2,3] impotence[2,3] and cold extremities[2-4]

Contraindicated in bronchial asthma, overt cardiac failure, greater-than-first-degree heart block, cardiogenic shock, and severe bradycardia.

See next page for references and Brief Summary of Product Information, which includes a listing of reported adverse reactions.

TRANDATE® b.i.d.

labetalol HCl/Glaxo 100 mg/200 mg tablets

Because it also vasodilates

References: 1. Holtzman JL, Finley D, Johnson B, et al: The effects of single-dose atenolol, labetalol, and propranolol on cardiac and vascular function. *Clin Pharmacol Ther* 1986;40:268-273. 2. Due DL, Giguere GC, Plachetka JR: Postmarketing comparison of labetalol and propranolol in hypertensive patients. *Clin Ther* 1986;8(6):624-631. 3. Burris JF, Goldstein J, Zager PG, et al: Comparative tolerability of labetalol versus propranolol, atenolol, pindolol, metoprolol, and nadolol. *J Clin Hypertens* 1986;3:1-9. 4. Erb RJ, Plachetka JR: Thermographic evaluation of the peripheral vascular effects of labetalol and propranolol. *Curr Ther Res* 1985;28(1):68-73.

TRANDATE® Tablets
(labetalol hydrochloride)

BRIEF SUMMARY OF PRODUCT INFORMATION

The following is a brief summary only. Before prescribing, see complete prescribing information in TRANDATE® Tablets product labeling.

INDICATIONS AND USAGE: TRANDATE® Tablets are indicated in the management of hypertension. TRANDATE Tablets may be used alone or in combination with other antihypertensive agents, especially thiazide and loop diuretics.

CONTRAINDICATIONS: TRANDATE® Tablets are contraindicated in bronchial asthma, overt cardiac failure, greater-than-first-degree heart block, cardiogenic shock, and severe bradycardia (see **WARNINGS**).

WARNINGS: Cardiac Failure: Sympathetic stimulation is a vital component supporting circulatory function in congestive heart failure. Beta-blockade carries a potential hazard of further depressing myocardial contractility and precipitating more severe failure. Although beta-blockers should be avoided in overt congestive heart failure, if necessary labetalol HCl can be used with caution in patients with a history of heart failure who are well compensated. Congestive heart failure has been observed in patients receiving labetalol HCl. Labetalol HCl does not abolish the inotropic action of digitalis on heart muscle.

In Patients Without a History of Cardiac Failure: In patients with latent cardiac insufficiency, continued depression of the myocardium with beta-blocking agents over a period of time can, in some cases, lead to cardiac failure. At the first sign or symptom of impending cardiac failure, patients should be fully digitalized and/or be given a diuretic, and the response should be observed closely. If cardiac failure continues despite adequate digitalization and diuretic, TRANDATE® therapy should be withdrawn (gradually, if possible).

Exacerbation of Ischemic Heart Disease Following Abrupt Withdrawal: Angina pectoris has not been reported upon labetalol HCl discontinuation. However, hypersensitivity to catecholamines has been observed in patients withdrawn from beta-blocker therapy; exacerbation of angina and, in some cases, myocardial infarction have occurred after *abrupt* discontinuation of such therapy. When discontinuing chronically administered TRANDATE, particularly in patients with ischemic heart disease, the dosage should be gradually reduced over a period of one to two weeks and the patient should be carefully monitored. If angina markedly worsens or acute coronary insufficiency develops, TRANDATE administration should be reinstituted promptly, at least temporarily, and other measures appropriate for the management of unstable angina should be taken. Patients should be warned against interruption or discontinuation of therapy without the physician's advice. Because coronary artery disease is common and may be unrecognized, it may be prudent not to discontinue TRANDATE therapy abruptly even in patients treated only for hypertension.

Nonallergic Bronchospasm (eg, Chronic Bronchitis and Emphysema): Patients with bronchospastic disease should, in general, not receive beta-blockers. TRANDATE may be used with caution, however, in patients who do not respond to, or cannot tolerate, other antihypertensive agents. It is prudent, if TRANDATE is used, to use the smallest effective dose, so that inhibition of endogenous or exogenous beta-agonists is minimized.

Pheochromocytoma: Labetalol HCl has been shown to be effective in lowering blood pressure and relieving symptoms in patients with pheochromocytoma. However, paradoxical hypertensive responses have been reported in a few patients with this tumor; therefore, use caution when administering labetalol HCl to patients with pheochromocytoma.

Diabetes Mellitus and Hypoglycemia: Beta-adrenergic blockade may prevent the appearance of premonitory signs and symptoms (eg, tachycardia) of acute hypoglycemia. This is especially important with labile diabetics. Beta-blockade also reduces the release of insulin in response to hyperglycemia; it may therefore be necessary to adjust the dose of antidiabetic drugs.

Major Surgery: The necessity or desirability of withdrawing beta-blocking therapy prior to major surgery is controversial. Protracted severe hypotension and difficulty in restarting or maintaining a heartbeat have been reported with beta-blockers. The effect of labetalol HCl's alpha-adrenergic activity has not been evaluated in this setting.

A synergism between labetalol HCl and halothane anesthesia has been shown (see **Drug Interactions** under **PRECAUTIONS**).

PRECAUTIONS: General: ***Impaired Hepatic Function:*** TRANDATE® Tablets should be used with caution in patients with impaired hepatic function since metabolism of the drug may be diminished.

Jaundice or Hepatic Dysfunction: On rare occasions, labetalol HCl has been associated with jaundice (both hepatic and cholestatic). It is therefore recommended that treatment with labetalol HCl be stopped immediately should a patient develop jaundice or laboratory evidence of liver injury. Both have been shown to be reversible on stopping therapy.

Information for Patients: As with all drugs with beta-blocking activity, certain advice to patients being treated with labetalol HCl is warranted. This information is intended to aid in the safe and effective use of this medication. It is not a disclosure of all possible adverse or intended effects. While no incidence of the abrupt withdrawal phenomenon (exacerbation of angina pectoris) has been reported with labetalol HCl, dosing with TRANDATE Tablets should not be interrupted or discontinued without a physician's advice. Patients being treated with TRANDATE Tablets should consult a physician at any sign of impending cardiac failure. Also, transient scalp tingling may occur, usually when treatment with TRANDATE Tablets is initiated (see **ADVERSE REACTIONS**).

Laboratory Tests: As with any new drug given over prolonged periods, laboratory parameters should be observed over regular intervals. In patients with concomitant illnesses, such as impaired renal function, appropriate tests should be done to monitor these conditions.

Drug Interactions: In one survey, 2.3% of patients taking labetalol HCl in combination with tricyclic antidepressants experienced tremor as compared to 0.7% reported to occur with labetalol HCl alone. The contribution of each of the treatments to this adverse reaction is unknown, but the possibility of a drug interaction cannot be excluded.

Drugs possessing beta-blocking properties can blunt the bronchodilator effect of beta-receptor agonist drugs in patients with bronchospasm; therefore, doses greater than the normal antiasthmatic dose of beta-agonist bronchodilator drugs may be required.

Cimetidine has been shown to increase the bioavailability of labetalol HCl. Since this could be explained either by enhanced absorption or by an alteration of hepatic metabolism of labetalol HCl, special care should be used in establishing the dose required for blood pressure control in such patients.

Synergism has been shown between halothane anesthesia and intravenously administered labetalol HCl. During controlled hypotensive anesthesia using labetalol HCl in association with halothane, high concentrations (3% or above) of halothane should not be used because the degree of hypotension will be increased and because of the possibility of a large reduction in cardiac output and an increase in central venous pressure. The anesthesiologist should be informed when a patient is receiving labetalol HCl.

Labetalol HCl blunts the reflex tachycardia produced by nitroglycerin without preventing its hypotensive effect. If labetalol HCl is used with nitroglycerin in patients with angina pectoris, additional antihypertensive effects may occur.

Drug/Laboratory Test Interactions: The presence of a metabolite of labetalol in the urine may result in falsely increased levels of urinary catecholamines when measured by a nonspecific trihydroxyindole (THI) reaction. In screening patients suspected of having a pheochromocytoma and being treated with labetalol HCl, specific radioenzymatic or high performance liquid chromatography assay techniques should be used to determine levels of catecholamines or their metabolites.

Carcinogenesis, Mutagenesis, Impairment of Fertility: Long-term oral dosing studies with labetalol HCl for 18 months in mice and for two years in rats showed no evidence of carcinogenesis. Studies with labetalol HCl using dominant lethal assays in rats and mice and exposing microorganisms according to modified Ames tests showed no evidence of mutagenesis.

Pregnancy: ***Teratogenic Effects: Pregnancy Category C:*** Teratogenic studies have been performed with

TRANDATE® Tablets (labetalol hydrochloride)

labetalol in rats and rabbits at oral doses up to approximately six and four times the maximum recommended human dose (MRHD), respectively. No reproducible evidence of fetal malformations was observed. Increased fetal resorptions were seen in both species at doses approximating the MRHD. There are no adequate and well-controlled studies in pregnant women. Labetalol should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus.

Nonteratogenic Effects: Infants of mothers who were treated with labetalol HCl during pregnancy did not appear to be adversely affected by the drug. Oral administration of labetalol to rats during late gestation through weaning at doses of two to four times the MRHD caused a decrease in neonatal survival.

Labor and Delivery: Labetalol HCl given to pregnant women with hypertension did not appear to affect the usual course of labor and delivery.

Nursing Mothers: Small amounts of labetalol (approximately 0.004% of the maternal dose) are excreted in human milk. Caution should be exercised when TRANDATE Tablets are administered to a nursing woman.

Pediatric Use: Safety and effectiveness in children have not been established.

ADVERSE REACTIONS: Most adverse effects are mild, transient, and occur early in the course of treatment. In controlled clinical trials of three to four months' duration, discontinuation of TRANDATE® Tablets due to one or more adverse effects was required in 7% of all patients. In these same trials, beta-blocker control agents led to discontinuation in 8% to 10% of patients, and a centrally acting alpha-agonist in 30% of patients.

The following adverse reactions were derived from multi-center, controlled clinical trials over treatment periods of three and four months. The rates, which ranged from less than 1% to 5% except as otherwise noted, are based on adverse reactions considered probably drug-related by the investigator. If all reports are considered, the rates are somewhat higher (eg, dizziness, 20%; nausea, 14%; fatigue, 11%).

Body as a Whole: Fatigue, asthenia, and headache.

Gastrointestinal: Nausea (6%), vomiting, dyspepsia, diarrhea, and taste distortion.

Central and Peripheral Nervous Systems: Dizziness (11%), paresthesia, and drowsiness.

Autonomic Nervous System: Nasal stuffiness, ejaculation failure, impotence, and increased sweating.

Cardiovascular: Edema and postural hypotension.

Respiratory: Dyspnea.

Skin: Rash.

Special Senses: Vision abnormality and vertigo.

The adverse effects were reported spontaneously and are representative of the incidence of adverse effects that may be observed in a properly selected hypertensive patient population, ie, a group excluding patients with bronchospastic disease, overt congestive heart failure, or other contraindications to beta-blocker therapy.

Clinical trials also included studies utilizing daily doses up to 2,400 mg in more severely hypertensive patients. The US therapeutic trials data base for adverse reactions that are clearly or possibly dose-related shows that the following side effects increased with increasing dose: dizziness, fatigue, nausea, vomiting, dyspepsia, paresthesia, nasal stuffiness, ejaculation failure, impotence, and edema.

In addition, a number of other less common adverse events have been reported in clinical trials or the literature:

Cardiovascular: Postural hypotension, including rarely, syncope.

Central and Peripheral Nervous Systems: Paresthesias, most frequently described as scalp tingling. In most cases, it was mild, transient, and usually occurred at the beginning of treatment.

Collagen Disorders: Systemic lupus erythematosus; positive antinuclear factor (ANF).

Eyes: Dry eyes.

Immunological System: Antimitochondrial antibodies.

Liver and Biliary System: Cholestasis with or without jaundice.

Musculoskeletal System: Muscle cramps; toxic myopathy.

Respiratory System: Bronchospasm.

Skin and Appendages: Rashes of various types, such as generalized maculopapular, lichenoid, urticarial, bullous lichen planus, psoriaform, and facial erythema; Peyronie's disease; reversible alopecia.

Urinary System: Difficulty in micturition, including acute urinary bladder retention.

Following approval for marketing in the United Kingdom, a monitored release survey involving approximately 6,800 patients was conducted for further safety and efficacy evaluation of this product. Results of this survey indicate that the type, severity, and incidence of adverse effects were comparable to those cited above.

Potential Adverse Effects: In addition, other adverse effects not listed above have been reported with other beta-adrenergic blocking agents.

Central Nervous System: Reversible mental depression progressing to catatonia, an acute reversible syndrome characterized by disorientation for time and place, short-term memory loss, emotional lability, slightly clouded sensorium, and decreased performance or neuropsychometrics.

Cardiovascular: Intensification of AV block (see **CONTRAINDICATIONS**).

Allergic: Fever combined with aching and sore throat; laryngospasm; respiratory distress.

Hematologic: Agranulocytosis; thrombocytopenic or nonthrombocytopenic purpura.

Gastrointestinal: Mesenteric artery thrombosis; ischemic colitis.

The oculomucocutaneous syndrome associated with the beta-blocker practolol has not been reported with labetalol HCl.

Clinical Laboratory Tests: There have been reversible increases of serum transaminases in 4% of patients treated with labetalol HCl and tested, and more rarely, reversible increases in blood urea.

OVERDOSAGE: Information concerning possible overdosage and its treatment appears in the full prescribing information.

DOSAGE AND ADMINISTRATION: DOSAGE MUST BE INDIVIDUALIZED. The recommended *initial* dosage is 100 mg *twice* daily whether used alone or added to a diuretic regimen. After two or three days, using standing blood pressure as an indicator, dosage may be titrated in increments of 100 mg bid every two or three days. The usual *maintenance* dosage of labetalol HCl is between 200 and 400 mg *twice* daily. Before use, see complete prescribing information for dosage details.

HOW SUPPLIED: TRANDATE® Tablets, 100 mg, light orange, round, scored, film-coated tablets engraved on one side with "TRANDATE 100 GLAXO," bottles of 100 (NDC 0173-0346-43) and 500 (NDC 0173-0346-44) and unit dose packs of 100 tablets (NDC 0173-0346-47).

TRANDATE Tablets, 200 mg, white, round, scored, film-coated tablets engraved on one side with "TRANDATE 200 GLAXO," bottles of 100 (NDC 0173-0347-43) and 500 (NDC 0173-0347-44) and unit dose packs of 100 tablets (NDC 0173-0347-47).

TRANDATE Tablets, 300 mg, peach, round, scored, film-coated tablets engraved on one side with "TRANDATE 300 GLAXO," bottles of 100 (NDC 0173-0348-43) and 500 (NDC 0173-0348-44) and unit dose packs of 100 tablets (NDC 0173-0348-47).

TRANDATE Tablets should be stored between 2° and 30°C (36° and 86°F). TRANDATE Tablets in the unit dose boxes should be protected from excessive moisture.

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September 1986

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Research Triangle Park, NC 27709

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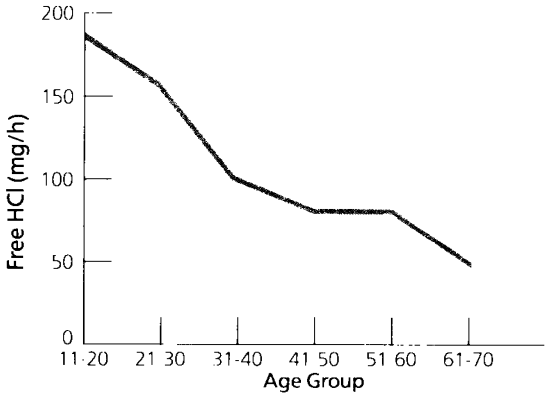
Specialized ulcer therapy

When advancing age signals reduced acid secretion

If your duodenal ulcer patient is over 55, decreased mucosal resistance is more likely to cause an ulcer than hypersecretion of acid-pepsin.[1] A tendency toward lower acid secretion with advancing age has been shown.[2,3]

Declining gastric secretion and age[3]



CARAFATE® (sucralfate/Marion) makes sense as initial ulcer therapy for the elderly. Carafate provides ulcer healing rates comparable to H_2 antagonists without the risk of systemic side effects or drug interactions—an important benefit for older patients.

The unique, nonsystemic action of Carafate enhances the body's own ulcer healing ability, strengthening the mucosal structure as it protects damaged tissue from further injury.

When advancing age signals reduced acid secretion, choose the specialized ulcer therapy of safe, nonsystemic Carafate.

Nothing works like

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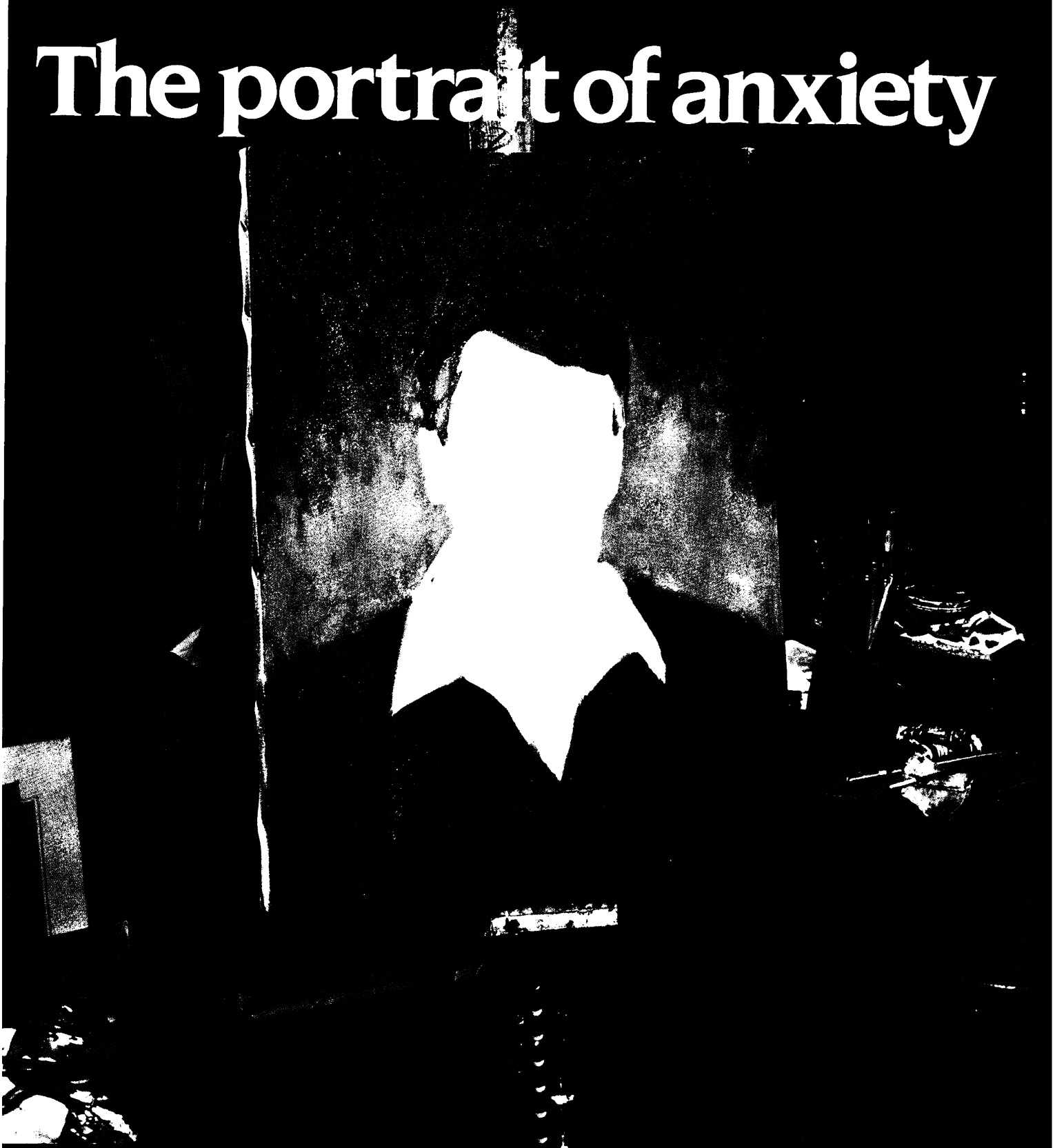
Please see adjoining page for references and brief summary of prescribing information.

1595H7

The portrait of anxiety



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Kalamazoo, Michigan 49001 USA

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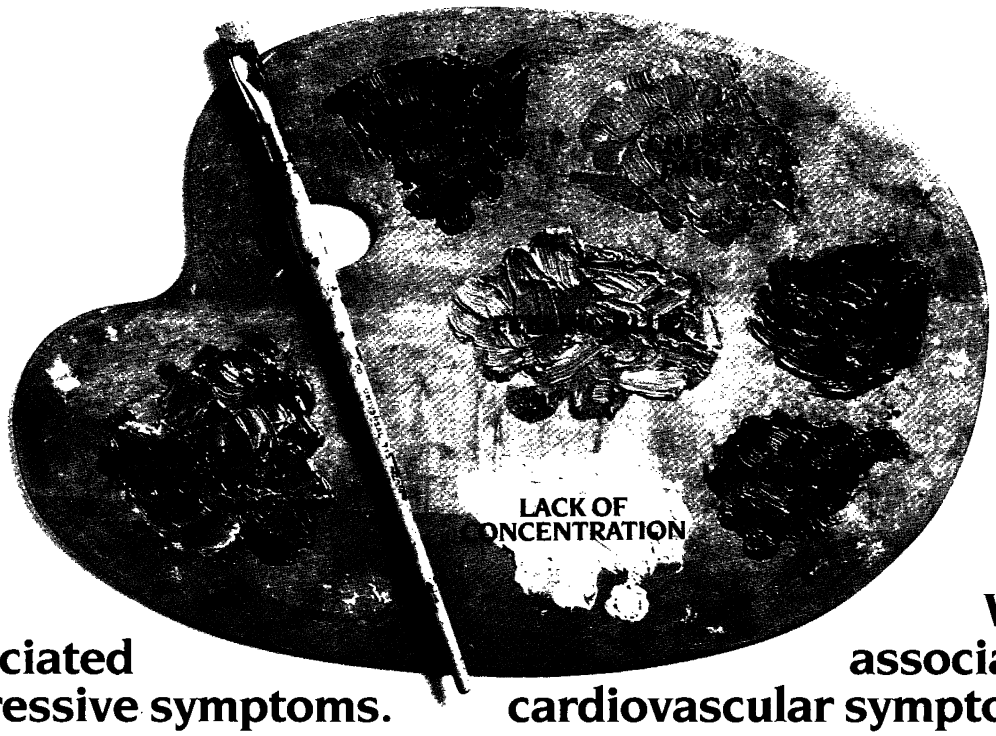
is often complicated



With associated depressive symptoms.

In double-blind, four-week clinical trials in 632 patients with moderate to severe anxiety, therapy with XANAX was compared with placebo.

XANAX was significantly more effective ($P<.001$) than placebo in relieving the anxiety, with over half of the patients showing marked to moderate improvement by the first evaluation period (one week).

In addition, over 70% of these patients experienced associated moderate to severe depressed mood. XANAX was shown to be significantly more effective ($P<.014$) than placebo in improving the associated depressed mood.

With associated cardiovascular symptoms.

Almost 60% of patients in the study had anxiety with associated cardiovascular symptoms even though cardiovascular disease had been ruled out. XANAX was shown to effectively relieve anxiety including the associated cardiovascular symptoms.

XANAX, the first of a unique class—the triazolobenzodiazepines.

- *Well tolerated*—Side effects, if they occur, are generally observed at the beginning of therapy and usually disappear with continued medication. Drowsiness and light-headedness were the most commonly reported adverse reactions.
- *Sustained efficacy*—No reported increase in dosage during 16-week clinical study, once an appropriate dosage was achieved. Since long-term effectiveness of XANAX has not been established, it is recommended that it not be used for longer than 16 weeks.
- *Simple dosage*—0.25 to 0.5 mg t.i.d.

TABLETS 0.25, 0.5 & 1 MG

Xanax®

alprazolam IV

for the relief of complicated anxiety

Your prescription now...

for a lifetime of happy dental visits

During the first months of life, Vi-Flor® vitamin-fluoride supplements begin to enhance tooth morphology,[1] increase enamel hardness, and promote mineralization of unerupted teeth[2]—all while providing recommended minimum daily amounts of selected vitamins.

Fluoride supplementation is both prophylactic *and* therapeutic, especially with newborns who are already in the process of developing 20 primary and 32 permanent teeth. In fact, receiving adequate systemic fluoride beginning the first months of life can help reduce childhood cavities by 50-80%.[3]

And that *daily* use through age 16 results in optimal levels of fluoride supplementation, for a lifetime of stronger teeth and lower-cost dental care.

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Vi-Flor® vitamin-fluoride supplements... now.
The essential first step begins with you, and...

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References:

1. Moss SJ: The worldwide decline in caries prevention, in Mead Johnson Clinical Report Series, Clinical Importance of Fluoride Nutrition in Infants, Children, and Young Adults. Chicago, Pragmaton® 1985, Number 1, p. 2.

2. Newbrun E: How fluoride works: Topical vs. systemic action, in Mead Johnson Clinical Report Series, Clinical Importance of Fluoride Nutrition in Infants, Children, and Young Adults. Chicago, Pragmaton® 1985, Number 1, p. 5.

3. Aasenden R and Peebles T: Effects of fluoride supplementation from birth on human deciduous and permanent teeth. *Arch Oral Biol* 1974;19:321.

Mead Johnson
NUTRITIONAL DIVISION

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L-K244-1-87

Routine VI-FLOR® supplementation

to help you guard appropriate patients against caries risk and nutritional risk.

INDICATIONS AND USAGE: Prophylaxis of vitamin deficiencies and dental caries in children and adults when fluoride of water supply does not exceed 0.7 ppm.[1,2,3] And, in the case of TRI-VI-FLOR® 0.25 mg Drops with Iron and POLY-VI-FLOR® Drops and Chewable Tablets with Iron, prophylaxis against iron deficiencies. Note: VI-FLOR Drops do not contain folic acid because the vitamin is not stable in liquid form.

PRECAUTIONS: Do not exceed recommended dose or give concurrently with other medications containing significant amounts of fluoride. Prolonged excessive fluoride intake may cause dental fluorosis. All VI-FLOR® with Iron products: as with all products containing iron, parents should be warned against excessive dosage. The bottle should be kept out of reach of children.

Keep all VI-FLOR with Iron products tightly closed and away from direct light.

VI-FLOR Drops should be dispensed in the original plastic container, since contact with glass leads to instability and precipitation.

ADVERSE REACTIONS: Allergic rash has rarely been reported.

DOSAGE AND ADMINISTRATION:
Supplemental Fluoride Dosage Schedule (mg/day)*

Age	Concentration of Fluoride in Drinking Water (ppm)		
	<0.3	0.3-0.7	>0.7
2-wk-2 yr**	0.25	0	0
2-3 yr	0.5	0.25	0
3-16 yr	1.0	0.5	0

*From the American Academy of Pediatrics Committee on Nutrition statement. Fluoride Supplementation: Revised Dosage Schedule. *Pediatrics* 63(1):150-152, 1979.
**The Committee favors initiating fluoride supplementation shortly after birth in breast-fed infants (0.25 mg F/day). In formula-fed infants, fluoride supplementation should be according to the fluoride content of the water used to prepare formula.

PRODUCT	FORM	SIZE	FLUORIDE mg/dose
POLY-VI-FLOR 0.25 mg	Drops	50 ml Bottle	0.25
POLY-VI-FLOR 0.25 mg with Iron	Drops	50 ml Bottle	0.25
POLY-VI-FLOR 0.25 mg	Tablets	Bottle of 100	0.25
POLY-VI-FLOR 0.25 mg with Iron	Tablets	Bottle of 100	0.25
POLY-VI-FLOR 0.5 mg	Drops	50 ml Bottle	0.5
POLY-VI-FLOR 0.5 mg with Iron	Drops	50 ml Bottle	0.5
POLY-VI-FLOR 0.5 mg	Tablets	Bottle of 100	0.5
POLY-VI-FLOR 0.5 mg with Iron	Tablets	Bottle of 100	0.5
POLY-VI-FLOR 1.0 mg	Tablets	Bottle of 100	1.0
POLY-VI-FLOR 1.0 mg with Iron	Tablets	Bottle of 100	1.0
TRI-VI-FLOR 0.25 mg	Drops	50 ml Bottle	0.25
TRI-VI-FLOR 0.25 mg with Iron	Drops	50 ml Bottle	0.25
TRI-VI-FLOR 0.5 mg	Drops	50 ml Bottle	0.5
TRI-VI-FLOR 1.0 mg	Tablets	Bottle of 100	1.0

REFERENCES:
1. Hennon DK, Stookey GK and Muhler JC: The Clinical Anticariogenic Effectiveness of Supplementary Fluoride-Vitamin Preparations—Results at the End of Four Years. *J Dentistry for Children* 34:439-443 (Nov) 1967.
2. Hennon DK, Stookey GK and Muhler JC: The Clinical Anticariogenic Effectiveness of Supplementary Fluoride-Vitamin Preparations—Results at the End of Five and a Half Years. *Pharmacology and Therapeutics in Dentistry* 1:1-6 (Oct) 1970.
3. Hennon DK, Stookey GK and Muhler JC: Prophylaxis of Dental Caries: Relative Effectiveness of Chewable Fluoride Preparations With and Without Added Vitamins. *J Pediatrics* 80:1018-1021 (June) 1972.

VI-SOL®/VI-FLOR® products are the nation's most prescribed children's vitamin and vitamin-fluoride supplements.

(For complete details, please consult full prescribing information.)

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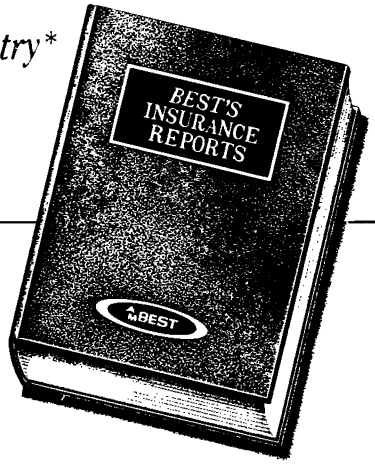

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Spare your patients the extra cost—in calories, sodium and dollars.

Spare your patients the rigors of dietary K^+ supplementation.

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25mg *Hydrochlorothiazide/***50mg** *Triamterene/SKF*

Effective antihypertensive* therapy...without the bananas

DAW
'DYAZIDE' AS WRITTEN.

* *Not for initial therapy. See brief summary.*

Before prescribing, see complete prescribing information in SK&F CO. literature or PDR. The following is a brief summary.

* **WARNING**

This drug is not indicated for initial therapy of edema or hypertension. Edema or hypertension requires therapy titrated to the individual. If this combination represents the dosage so determined, its use may be more convenient in patient management. Treatment of hypertension and edema is not static, but must be reevaluated as conditions in each patient warrant.

Contraindications: *Concomitant use with other potassium-sparing agents such as spironolactone or amiloride. Further use in anuria, progressive renal or hepatic dysfunction, hyperkalemia. Pre-existing elevated serum potassium. Hypersensitivity to either component or other sulfonamide-derived drugs.*

Warnings: Do not use potassium supplements, dietary or otherwise, unless hypokalemia develops or dietary intake of potassium is markedly impaired. *If supplementary potassium is needed, potassium tablets should not be used. Hyperkalemia can occur, and has been associated with cardiac irregularities. It is more likely in the severely ill, with urine volume less than one liter/day, the elderly and diabetics with suspected or confirmed renal insufficiency. Periodically, serum K^+ levels should be determined. If hyperkalemia develops, substitute a thiazide alone, restrict K^+ intake.* ***Associated widened QRS complex or arrhythmia requires prompt additional therapy.*** *Thiazides cross the placental barrier and appear in cord blood. Use in pregnancy requires weighing anticipated benefits against possible hazards, including fetal or neonatal jaundice, thrombocytopenia, other adverse reactions seen in adults. Thiazides appear and triamterene may appear in breast milk. If their use is essential, the patient should stop nursing. Adequate information on use in children is not available. Sensitivity reactions may occur in patients with or without a history of allergy or bronchial asthma. Possible exacerbation or activation of systemic lupus erythematosus has been reported with thiazide diuretics.*

Precautions: *The bioavailability of the hydrochlorothiazide component of 'Dyazide' is about 50% of the bioavailability of the single entity. Theoretically, a patient transferred from the single entities of triamterene and hydrochlorothiazide may show an increase in blood pressure or fluid retention. Similarly, it is also possible that the lesser hydrochlorothiazide bioavailability could lead to increased serum potassium levels. However, extensive clinical experience with 'Dyazide' suggests that these conditions have not been commonly observed in clinical practice. Angiotensin-converting enzyme (ACE) inhibitors can elevate serum potassium; use with caution with 'Dyazide'. Do periodic serum electrolyte determinations (particularly important in patients vomiting excessively or receiving parenteral fluids, and during concurrent use with amphotericin B or corticosteroids or corticotropin[ACTH]). Periodic BUN and serum creatinine determinations should be made, especially in the elderly, diabetics or those with suspected or confirmed renal insufficiency. Cumulative effects of the drug may develop in patients with impaired renal function. Thiazides should be used with caution in patients with impaired hepatic function. They can precipitate coma in patients with severe liver disease. Observe regularly for possible blood dyscrasias, liver damage, other idiosyncratic reactions. Blood dyscrasias have been reported in patients receiving triamterene, and leukopenia, thrombocytopenia, agranulocytosis, and aplastic and hemolytic anemia have been reported with thiazides. Thiazides may cause manifestation of latent diabetes mellitus. The effects of oral anticoagulants may be decreased when used concurrently with hydrochlorothiazide; dosage adjustments may be necessary. Clinically insignificant reductions in arterial responsiveness to norepinephrine have been reported. Thiazides have also been shown to increase the paralyzing effect of nondepolarizing muscle relaxants such as tubocurarine. Triamterene is a weak folic acid antagonist. Do periodic blood studies in cirrhotics with splenomegaly. Antihypertensive effects may be enhanced in post-sympathectomy patients. Use cautiously in surgical patients. Triamterene has been found in renal stones in association with the other usual calculus components. Therefore, 'Dyazide' should be used with caution in patients with histories of stone formation. A few occurrences of acute renal failure have been reported in patients on 'Dyazide' when treated with indomethacin. Therefore, caution is advised in administering nonsteroidal anti-inflammatory agents with 'Dyazide'. The following may occur: transient elevated BUN or creatinine or both, hyperglycemia and glycosuria (diabetic insulin requirements may be altered), hyperuricemia and gout, digitalis intoxication (in hypokalemia), decreasing alkali reserve with possible metabolic acidosis. 'Dyazide' interferes with fluorescent measurement of quinidine. Hypokalemia is uncommon with 'Dyazide', but should it develop, corrective measures should be taken such as potassium supplementation or increased dietary intake of potassium-rich foods. Corrective measures should be instituted cautiously and serum potassium levels determined. Discontinue corrective measures and 'Dyazide' should laboratory values reveal elevated serum potassium. Chloride deficit may occur as well as dilutional hyponatremia. Concurrent use with chlorpropamide may increase the risk of severe hyponatremia. Serum PBI levels may decrease without signs of thyroid disturbance. Calcium excretion is decreased by thiazides. 'Dyazide' should be withdrawn before conducting tests for parathyroid function. Thiazides may add to or potentiate the action of other antihypertensive drugs. Diuretics reduce renal clearance of lithium and increase the risk of lithium toxicity.*

Adverse Reactions: *Muscle cramps, weakness, dizziness, headache, dry mouth; anaphylaxis, rash, urticaria, photosensitivity, purpura, other dermatological conditions; nausea and vomiting, diarrhea, constipation, other gastrointestinal disturbances; postural hypotension (may be aggravated by alcohol, barbiturates, or narcotics). Necrotizing vasculitis, paresthesias, icterus, pancreatitis, xanthopsia and respiratory distress including pneumonitis and pulmonary edema, transient blurred vision, sialadenitis, and vertigo have occurred with thiazides alone. Triamterene has been found in renal stones in association with other usual calculus components. Rare incidents of acute interstitial nephritis have been reported. Impotence has been reported in a few patients on 'Dyazide', although a causal relationship has not been established.*

Supplied: 'Dyazide' is supplied as a red and white capsule, in bottles of 1000 capsules; Single Unit Packages (unit-dose) of 100 (intended for institutional use only); in Patient-Pak™ unit-of-use bottles of 100.

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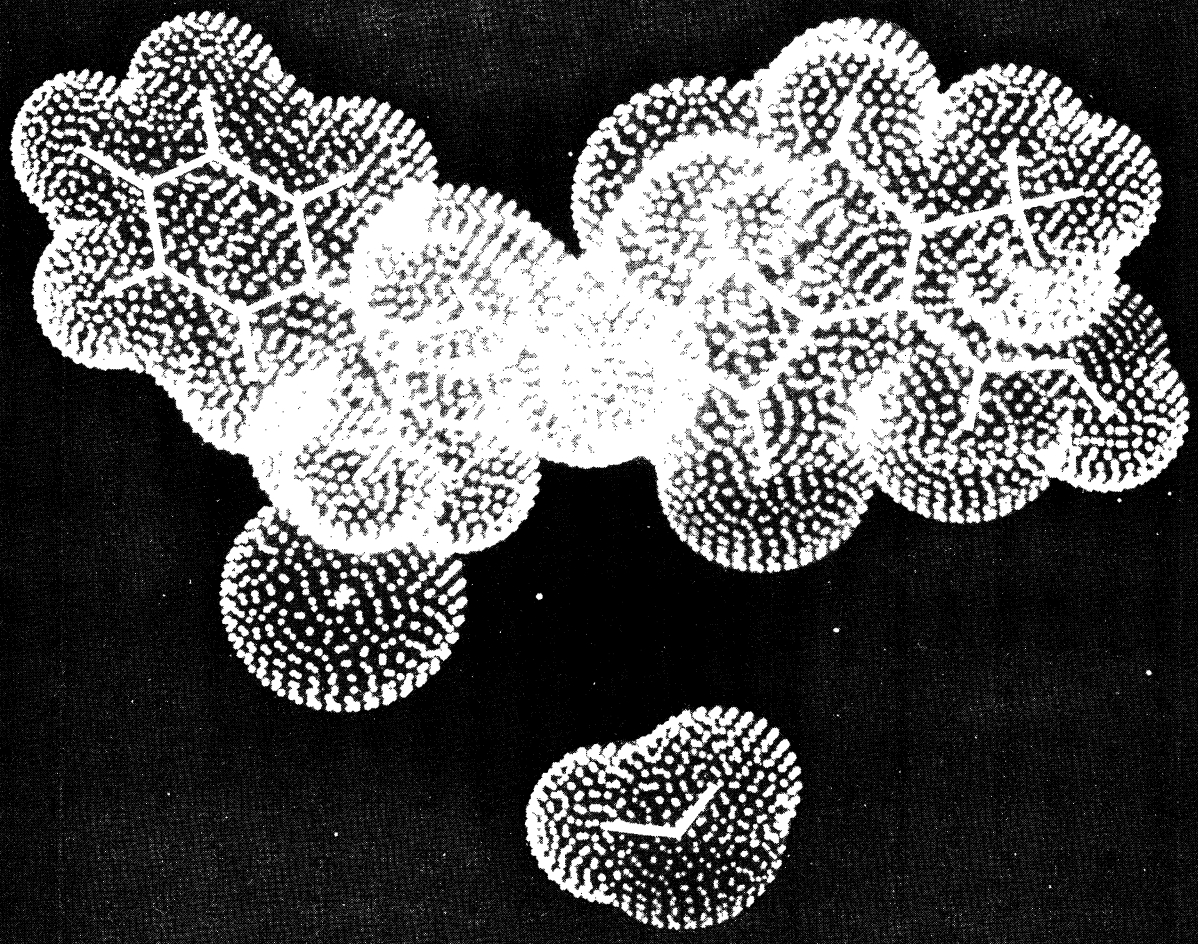

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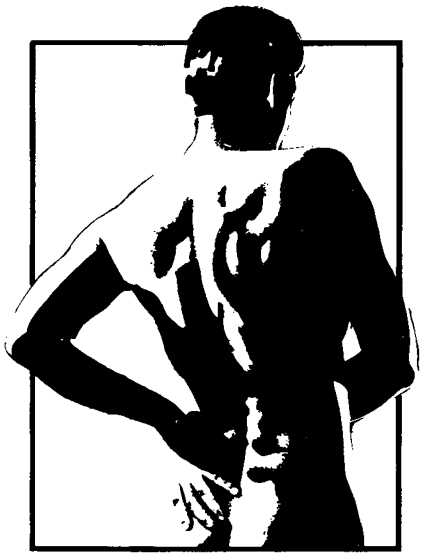
Computer-generated molecular structure of cephalexin hydrochloride monohydrate



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NEUROLOGIST. Visalia Medical Clinic, Inc, a 37 physician multispecialty group, is searching for a Neurologist to enter an active practice. Located in the San Joaquin Valley in California and serving a market area of approximately 350,000. Excellent hospital services and facilities. BC/BE. Compensation is incentive oriented with rapid advancement to full partnership. Excellent fringe benefits. Please respond to John G. Heinsohn, Administrator, 5400 W. Hillsdale, Visalia, CA 93291; (209) 733-5222.

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OB/GYN. Multispecialty group in northwest Washington desires second Obstetrician. Excellent practice opportunity, full range of benefits, early partnership status, all practice costs paid. For more information contact Shane Spray, Administrator, 1400 E. Kincaid, Mount Vernon, WA 98273; (206) 428-2524.

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CALIFORNIA. Emergency Medicine Faculty Positions. Immediate opportunities available for career-oriented Emergency Physicians who possess excellent clinical and teaching skills to join the faculty of Emergency Medicine department. BC in Family Practice, Internal Medicine, Surgery, and/or BE in Emergency Medicine. Our facility, located in southern California, averages 38,000 Emergency department visits per year, is a level II trauma center, regional burn center and neonatology intensive care center. These positions require a teaching commitment in a university-affiliated Family Practice training program. We offer a competitive remuneration package to include salary, malpractice insurance, time off, and flexible scheduling. Send CV to Empire Medical Group, PO Box 3571, San Bernardino, CA 92413.

NEUROSURGERY. Visalia Medical Clinic has an opening for a BC/BE Neurological Surgeon to enter an immediate and active practice. Located in the San Joaquin Valley of California, serving a market area of approximately 350,000 citizens. Two Neurosurgeons presently serving this area. Excellent hospital services and facilities. Must be BC/BE. Compensation is incentive oriented with advancement to full partnership after one year. Excellent fringe benefits. John G. Heinsohn, Administrator, 5400 W. Hillsdale, Visalia, CA 93291; (209) 733-5222.

FAMILY PRACTITIONER. Visalia Medical Clinic has an opening for a BC/BE Family Practitioner to join a four physician department. Located in the San Joaquin Valley of California, serving a market area of approximately 350,000 citizens, the Visalia Medical Clinic is a 40 physician multispecialty clinic. Excellent hospital services and facilities. Compensation is incentive oriented with advancement to full partnership after one year. Excellent fringe benefits. John G. Heinsohn, Administrator, 5400 W. Hillsdale, Visalia, CA 93291; (209) 733-5222.

INTERNIST. To join two Primary Care Internists in private practice in beautiful far-northern California one hour below major center. Midway between Portland and San Francisco, we have a rural setting with sophisticated practice and excellent hospital facilities. Subspecialty interest desirable within primary care framework. Salary and benefits with partnership an early goal. CV and your interests to R. H. Alley, Jr, MD, 105 Oberlin Rd, Yreka, CA 96097.

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FULL AND PART-TIME PHYSICIANS

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NEAR STANFORD. Six Internists, all subspecialty trained and members of clinical faculty at Stanford, interested in an Associate with subspecialty interest and training. Should be well grounded in Internal Medicine. Send CV to Dr Bigler, El Camino Internal Medical Group, 125 South Dr, Mountain View, CA 94040.

BC/BE INTERNIST to associate with General Surgeon, OB/GYN, Pediatrician, Internist, and three FPs in well-established rural practice. Send CV to R. F. LeBlond, MD, Park Clinic, Box 1139, Livingston, MT 59047.

GENERAL INTERNIST needed for large hospital-based multispecialty clinic. University associated residency program. Attractive salary and complete benefit package. Pleasant setting. BC/BE. California license required. Contact Dennis L. Ostrem, MD, Chief Internal Medicine, The Permanente Medical Group, Inc, PO Box 254999, Sacramento, CA 95865-4999 or call (916) 973-5781. An Equal Opportunity Employer.

ARIZONA INTERNAL MEDICINE PHYSICIAN to associate with two man Internal Medicine group in Tucson. New office building with lab and x-ray. Well established practice. Sub-specialties welcome, BC/BE. Send CV to A. Oaks, 5265 E. Knight Dr, Tucson, AZ 85712.

EMERGENCY GROUP seeking career oriented ACLS, ATLS physician for immediate opening. Moderate volume, income $120,000. Great outdoor activities including fishing, boating, skiing and sailing in south central Washington. Send CV to KEP, PO Box 6192, Kennewick, WA 99336; or call (509) 627-1798.

UNIVERSITY OF CALIFORNIA, Irvine, Department of Medicine is seeking a full-time faculty person as General Internist for expanding academic group practice. Combined fee-for-service/capitation. Duties include 80-90% clinical practice in multispecialty faculty clinic, 10-20% teaching residents and students ambulatory care and inpatient medicine. Division of General Internal Medicine with strong commitment to teaching, practice, and research. Competitive salary and benefits. Affirmative action/equal opportunity employer. Send CV to Jeremiah Tilles, MD, UCI, Department of Medicine, Route 81, 101 City Drive South, Orange, CA 92668.

(Continued on Page 368)

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(Continued from Page 366)

PHYSICIANS WANTED

ORTHOPEDIST. The west coast's leading Occupational/Family Practice medical provider has FT/PT opportunities for Orthopedic Specialists in California and Washington (Seattle/Tacoma). Attractive package includes: guaranteed salary, incentive bonus and benefits. Current license. Contact Personnel Director, ReadiCare, Inc, 446 Oakmead Parkway, Sunnyvale, CA 94086; (800) 237-3234. Join our dynamic team of professionals. Practice and live in an incomparable environment.

CRESCENT CITY, CALIFORNIA. Exciting position available at a growing 24,000-visit ER in a rural, coastal community. Fee-for-service with possibility of six figure income. Send CV to Art B. Wong, MD, FACEP, 1 Maritime Plaza, Ste 710, San Francisco, CA 94111.

EMERGENCY MEDICINE. We are an established 35-physician partnership in northern California and we are seeking BE/BC Emergency Physicians to join us. All of our facilities have moderate volumes, many serve as EMS base-stations. Salary and benefits are competitive; malpractice is paid. If interested in a career in Emergency Medicine with us, please contact Sacramento Emergency Medical Group, 4325 Auburn Blvd, Ste 100, Sacramento, CA 95841; (916) 486-4414.

CARDIOLOGIST. BC/BE sought to join a large hospital-based multispecialty clinic. University affiliated residency program. Excellent fringe benefits. Competitive salary. California license required. Send CV to Aung-Win Chiong, MD, The Permanente Medical Group, Inc, PO Box 254999, Sacramento, CA 95865-4999, or call (916) 973-5748. An Equal Opportunity Employer.

INTERNIST. Immediate opening for a BC/BE General Internist to join a 35-member multispecialty group located in San Luis Obispo on the central coast. Benefits include immediate shareholder status, retirement program, all practice costs paid, starting guaranteed salary plus strong incentive plan. Send CV to Recruitment, San Luis Medical Clinic, Ltd., 1235 Osos St, San Luis Obispo, CA 93401-3619.

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NORTHERN SAN FRANCISCO BAY AREA: Seeking Physician BC/BE in Internal Medicine for Internist position in growing department. Kaiser Permanente Medical Center, 1550 Gateway Blvd, Fairfield, CA 94533; (707) 427-4200.

FELLOWSHIP IN GERIATRIC MEDICINE. A unique fellowship in Geriatric Medicine is being offered beginning July 1, 1988, by a Fortune 100 company and a major university medical school in California. The program is two years in duration and provides the gamut of geriatric health care experience and qualifies one for the certificate examination in Geriatric Medicine. The fellowship stipend is attractive as are the working conditions in this unique experience. For further information please contact Number 86, Western Journal of Medicine, PO Box 7602, San Francisco, CA 94120-7602.

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This newly created post (R4 or R5 level) is available July 1988 in the Internal Medicine Resident Training Program at Emanuel Hospital & Health Center. The Chief Resident's primary responsibility will be to provide academic assistance and leadership for 24 residents on the medicine service. Conference organization, morning report, bedside teaching, instruction in invasive procedures and duty schedule coordination are important parts of the job, but there will be ample time and abundant material for clinical research and publication. This post offers excellent preparation for a teaching career, subspecialty fellowship, or private practice in the Portland area. Send CV to Tony Andrews, PhD, FRCP, Chief of Medicine, Emanuel Hospital & Health Center, 2801 N. Gantenbein Ave, Portland, OR 97227; or call (503) 280-4384. Please include a daytime phone number.

PHYSICIANS WANTED. A General Surgeon and an Oncologist to join 16 physician multispecialty group with attached 40-bed hospital located in southern Idaho. Contact Business Administrator, Box 1233, Twin Falls, ID 83301.

NORTHERN CALIFORNIA rural community clinic seeks BC/BE Family Physician. Heart of the redwoods. Full range of practice, community hospital nearby. Contact Allan Katz, (707) 923-2783.

INVASIVE/NONINVASIVE CARDIOLOGIST. Full-time Cardiologist needed. Salaried position with excellent benefits. Send CV to Lancaster Cardiology Medical Group, Inc, 43847 N. Heaton Ave, Lancaster, CA 93534.

PACIFIC NORTHWEST. BE/BC Pediatrician wanted to join two Pediatricians in busy migrant health clinic. Family oriented community. Rural lifestyle. Excellent recreation. Negotiable salary, includes malpractice. Contact Ann Garza, YVFWC, PO Box 190, Toppenish, WA 98948; (509) 865-5600.

GENERAL SURGERY. Kaiser Permanente office in central California, rapidly growing new market area, seeking BC/BE specialty physicians in General Surgery. Address inquiries to Larry L. Coble, MD, Kaiser Permanente, 4785 N. First St, Fresno, CA 93726; (209) 221-4825.

ORTHOPEDICS. Kaiser Permanente office in central California, rapidly growing new market area, seeking BC/BE specialty physicians in Orthopedics. Address inquiries to Larry L. Coble, MD, Kaiser Permanente, 4785 N. First St, Fresno, CA 93726; (209) 221-4825.

INTERNAL MEDICINE. San Ysidro Health Center, a comprehensive multispecialty clinic in south San Diego County, seeks an Internist for full-time work. Competitive salary, excellent benefits. Send résumé to Norma Diaz, 4004 Beyer Blvd, San Ysidro, CA 92073; (619) 428-4463 ext 361.

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Enjoy professional challenge and growth with a successful and expanding HMO in southern California. CIGNA Healthplans of California is seeking Specialists and Primary Care physicians committed to concepts of prevention and health maintenance to join our facilities in Los Angeles and Orange Counties. We offer an excellent compensation and benefits package including profit sharing. For consideration, please forward CV to:

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(Continued on Page 370)

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(Continued from Page 368)

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FAMILY PRACTICE. Rural Colorado. BC/BE Family Practitioner to join three Family Practitioners in growing multispecialty group. Excellent opportunity for person interested in rural living, mountain recreation, health care delivery for medically underserved populations. Send CV to Michael Bloom, 204 Carson Ave, Alamosa, CO 81101; (303) 589-5161.

WALK-IN PHYSICIAN WANTED. ER/Primary Care training preferred, outstanding opportunity to start new department in rapidly growing multispecialty fee-for-service clinic in east San Gabriel Valley. Excellent salary and incentives. Send CV to Mr Ghormley, Administrator, 420 W. Rowland, Covina, CA 91723.

GENERAL INTERNIST position available with multispecialty group; BE/BC required; strong incentive plan; benefits included; retirement program and located in San Luis Obispo, California on the central coast. Send CV to Administration/Recruitment, San Luis Medical Clinic, 1235 Osos St, San Luis Obispo, CA 93401.

PEDIATRICIAN position available with multispecialty group; BE/BC required; strong incentive plan; benefits included; retirement program and located in San Luis Obispo, California on the central coast. Send CV to Administration/Recruitment, San Luis Medical Clinic, 1235 Osos St, San Luis Obispo, CA 93401.

OBSTETRICS/GYNECOLOGY. Kaiser Permanente office in central California, rapidly growing new market area, seeking BC/BE specialty physicians in OB/GYN. Address inquiries to Larry L. Coble, MD, Kaiser Permanente, 4785 N. First St, Fresno, CA 93726; (209) 221-4825.

PHYSICIANS WANTED

FAMILY PRACTITIONER. San Ysidro Health Center, a comprehensive multispecialty clinic in south San Diego County, seeks a Family Practitioner for full-time work. Competitive salary, excellent benefits. Send résumé to Norma Diaz, 4004 Beyer Blvd, San Ysidro, CA 92073; (619) 428-4463 ext 361.

Western States OPENINGS

Many multispecialty groups and hospitals have asked us to recruit for over 300 positions of various specialties. Both permanent and locum tenens. Send CV to:
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407 S. Clovis Ave, Ste 108, Fresno, CA 93727.
Or call (209) 252-3000.

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CENTRAL OREGON community seeks BE/BC Internist. 103-bed combination facility has ICU/CCU. Service area of 12,000. Coverage available by Internal Medicine group in neighboring town. Generous practice assistance package. An outdoorsman's winter and summer paradise! Contact Jean Erickson, PROSEARCH, 305 NE 102nd Ave, Portland, OR 97220; (503) 256-2070.

NORTHWEST WASHINGTON STATE. BC/BE Internist with intensive care skills to join young solo Internist in very busy practice. Consultations and primary care. Beautiful location, recreational activities, excellent lifestyle. Send CV to Number 93, Western Journal of Medicine, PO Box 7602, San Francisco, CA 94120-7602.

CARDIOLOGIST. The University of California, San Francisco and the Central California Faculty Medical Group seek a staff Cardiologist to join the teaching faculty at their affiliate, Valley Medical Center of Fresno. Applicants should be BC/BE. The scope of practice at VMC includes full invasive and non-invasive cardiology services. Geographic location offers a large population with a variety of cardiological diseases. VMC has 350 active beds and conducts residency training programs in most major clinical disciplines. The central California location offers enjoyable and affordable California living. Competitive salary and benefits. UCSF is an equal opportunity employer. Address inquiries to Lauren Grayson, MD, Chief of Cardiology, CCFMG, 2212 N. Winery, #130, Fresno, CA 93703; (209) 252-1835.

GENERAL SURGEON, BE/BC. Outstanding opportunity for aggressive surgeon with a highly profitable, well-established, fee-for-service, multispecialty clinic. 14 physicians on staff. Ready made practice. Unmatchable guaranteed salary first year, then ownership. New hospital. Wonderful family town with nationally recognized school system and unequalled outdoor recreation possibilities. Telephone calls will not be accepted. Send CV to John Brust, Mesaba Clinic, 1814 14th Ave East, Hibbing, MN 55746.

GASTROENTEROLOGIST position available with multispecialty group; BE/BC required; strong incentive plan; benefits included; retirement program and located in San Luis Obispo, California on the central coast. Send CV to Administration/Recruitment, San Luis Medical Clinic, 1235 Osos St, San Luis Obispo, CA 93401.

INTERNIST/NEPHROLOGIST with special interest in teaching Internal Medicine for full-time appointment in university-affiliated, active teaching and clinical program with part-time Nephrology private practice. Inquiries, including CV, should be sent to M.B. Ross, MD, Chairman, Department of Medicine, San Bernardino County Medical Center, 780 E. Gilbert St, San Bernardino, CA 92404.

PHYSICIANS WANTED

DERMATOLOGY. Kaiser Permanente office in central California, rapidly growing new market area, seeking BC/BE specialty physicians in Dermatology. Address inquiries to Larry L. Coble, MD, Kaiser Permanente, 4785 N. First St, Fresno, CA 93726; (209) 221-4825.

FAMILY PRACTITIONER position available with multispecialty group; BE/BC required; strong incentive plan; benefits included; retirement program and located in San Luis Obispo, California on the central coast. Send CV to Administration/Recruitment, San Luis Medical Clinic, 1235 Osos St, San Luis Obispo, CA 93401.

WEST AND SOUTHWEST. Locum tenens and permanent positions are now being offered to qualified Family Practitioners and other specialists in a wide variety of community and practice settings. Practice trials also an option. For more information with no obligation, contact your colleagues at physician-owned PRN, Limited, one of America's best established and most respected physician search firms. 1 (800) 531-1122. Ken Teufel, MD, PRN, Ltd., 1000 N. Walnut St, Ste B, New Braunfels, TX 78130.

CALIFORNIA. Internal Medicine. Full range of medicine. Solo, partnership, or group. Nice community surrounded by the mountains. Easy equal access to San Francisco, Los Angeles, beach, or skiing. No smog or fog, just great weather. Excellent financials and support. Contact Jeffrey Gowan at Merritt, Hawkins & Associates, 500 N. Newport Blvd, Ste 204, Newport Beach, CA 92663 or call (714) 548-0220.

CALIFORNIA. Family Practice. Full range of medicine. Solo, partnership, or group. Nice community surrounded by the mountains. Easy equal access to San Francisco, Los Angeles, beach, or skiing. No smog or fog, just great weather. Excellent financials and support. Contact Jeffrey Gowan at Merritt, Hawkins & Associates, 500 N. Newport Blvd, Ste 204, Newport Beach, CA 92663 or call (714) 548-0220.

PHYSICIANS NEEDED for immediate employment in non-surgical hemorrhoid treatment facility. 30 hours per week. Attractive salary package. Send résumé to Dr G. Green, PO Box 12565-W, Reno, NV 89510-2565.

RADIOLOGIST needed part-time to read office x-rays for large musculoskeletal group in Sacramento, California. Fees negotiable. Send CV to Number 90, Western Journal of Medicine, PO Box 7602, San Francisco, CA 94120-7602.

ORTHOPEDIC SURGEONS, BE/BC, general ortho or with spine, knee, hand, sports medicine fellowship, wanted for immediate openings in Sacramento, California, musculoskeletal specialty group. Guarantee, malpractice insurance, vacation first year, fee-for-service thereafter plus partnership opportunity. Interested physicians send CV to Number 91, Western Journal of Medicine, PO Box 7602, San Francisco, CA 94120-7602.

THE UNIVERSITY OF WASHINGTON seeks Assistant Professor in Nephrology to establish independent research program in molecular biology of renal diseases. Must be BC in Internal Medicine and BC/BE in Nephrology, qualified to provide clinical care and teach in Internal Medicine and Nephrology, trained for three plus years in renal cell biology with molecular biology experience and have independent grant or career development award. The University of Washington is an EOE. Please reply to Number 88, Western Journal of Medicine, PO Box 7602, San Francisco, CA 94120-7602.

FAMILY PHYSICIAN. BC/BE to join the Family Practice department of a busy, primary care based multispecialty group. Excellent opportunity for growth. Contact Shane Spray, Administrator, Skagit Valley Medical Center, 1400 E. Kincaid, Mt. Vernon, WA 98273; (206) 428-2524.

(Continued on Page 376)

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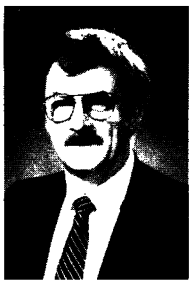

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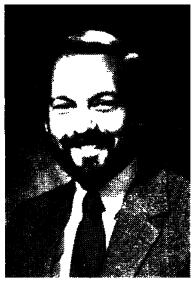

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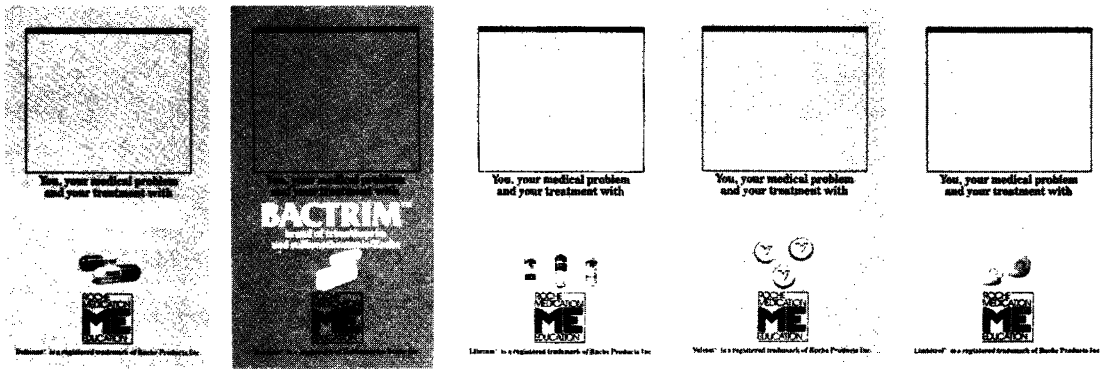

Medicines that matter from people who care

(Continued from Page 370)

PHYSICIAN WANTED

Our community-based, non-profit primary care medical group on the East side of Los Angeles has several highly visible positions available for qualified candidates:

Medical Director

You will be responsible for the administration of multiple clinic sites, and management and motivation of other physicians and staff. The selected candidate will have several years private practice experience and familiarity with both fee-for-service and prepaid medical practices. Fluency in medical Spanish would be preferred.

Physicians

We have both full and part time opportunities available in Family Practice, Internal Medicine, Pediatrics and OB/GYN.

In return for your expertise, our organization provides a competitive and comprehensive compensation package. For consideration, please forward a C.V. with salary history to: Jorgensen & Associates, 5134 Finehill, La Crescenta, CA 91214.

CAMARILLO (Ventura County). Multispecialty group of 35 physicians has immediate positions available for BC/BE Family Practitioner. This opening is located in the Camarillo satellite with the main facility located in Ventura. The growth oriented group is located on the California coast, 60 miles north of Los Angeles. Guaranteed salary plus incentives. No investment required. City is a great place to raise a family in a clean environment. Send résumé to Recruitment, Family Practice, 2705 Loma Vista Rd, Ventura, CA 93003.

VENTURA (Ventura County). Multispecialty group of 35 physicians has immediate position available for BC/BE Family Practitioner. This opening is located in the Immediate Care department. The growth oriented group is located on the California coast, 60 miles north of Los Angeles. Guaranteed salary plus incentives. No investment required. City is a great place to raise a family in a clean environment. Send résumé to Recruitment, Family Practice, 2705 Loma Vista Rd, Ventura, CA 93003.

AGGRESSIVE, BC or recently Board eligible Internist needed for fee-for-service, multispecialty group. New, fully equipped, 150-bed hospital with heliport. The area has excellent recreational facilities and superb family environment with a nationally recognized school system. Subspecialty support is provided under a University of Minnesota affiliation. Send CV to Mesaba Clinic, 1814 14th Ave East, Hibbing, MN 55746; Attention: J. Brust.

VENTURA (Ventura County). Multispecialty group of 35 physicians has immediate positions available for BC/BE General Internists. The growth oriented group is located on the California coast, 60 miles north of Los Angeles. Guaranteed salary plus incentives. No investment required. City is a great place to raise a family in a clean environment. Send résumé to Recruitment, General Internists, 2705 Loma Vista Rd, Ventura, CA 93003.

PHYSICIANS WANTED

CALIFORNIA

Primary care physicians needed to work as *locum tenens* in northern California. Radiologists needed statewide. High salary, paid malpractice. Work whenever you like. Permanent placements as well. Contact Carol Sweig, Director, (415) 673-7676.

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NEW MEXICO. BC/BE Primary Care Physician for 500-bed Psychiatric/Geriatric hospital. Exciting programs in an exciting location, with superb climate, recreational, and cultural benefits. Base salary $70,017 plus optional on-call salary supplement to $10,000. Fringe benefits are 21%, including paid malpractice and license fees, 2.5% per year retirement. Contact Philip Taulbee, MD, Medical Director, Las Vegas Medical Center, Box 1388, Las Vegas, NM 87701; (505) 454-2401.

LOS ANGELES. Part-time. Busy Occupational/Urgent Care Clinic seeks EM/FP caring professional 24-32 hours per week. Competitive compensation. Ted Angus, MD, 10720 So. Paramount Blvd, Downey, CA 90241.

FAMILY PHYSICIAN needed in northern New Mexico. Prime opportunity for BE/BC Family Physician looking for a challenge. Contact NM Health Resources, PO Box 27650, Albuquerque, NM 87125; (505) 242-0633.

PEDIATRICIAN. Large multispecialty group in San Francisco bay area seeks BC/BE full-time Pediatrician to join a growing practice. Attractive salary and benefits. Send CV to Fremont Medical Clinic, 39111 Paseo Padre Parkway, Ste 203, Fremont, CA 94538; Attention: Joy.

CALIFORNIA MOUNTAINS. Family Practice, community of 5,000 people needs a Family Physician to join the staff of their 26-bed acute care facility, full range of practice, income potential in the 100's, rural atmosphere in the scenic Sierra Nevada Mountains. For more information call David King collect at (714) 548-0220 or send CV to 500 N. Newport Blvd, Ste 204, Newport Beach, CA 92663.

FAMILY PHYSICIAN. UTAH IS BLOOMING—DISCOVER IT. Multispecialty practice currently has a position for a BC/BE Family Physician to join established group (three Family Practitioners, OB, two Pediatricians, General Surgeon); 35 miles/45 minutes from Salt Lake City; income guaranteed/excellent benefits; excellent outdoor recreational opportunities. Contact Dorothy Leonelli, Administrator, Family Practice Group, 255 South First East, Tooele, UT 84074; (801) 882-0424.

PEDIATRICIAN, BC/BE. Interest in Neonatology preferred. Attractive salary and benefits. Partnership available in two years. Busy practice in agricultural community one-and-one-half hours from San Diego, California. Reply with CV to Drs Mirza R. Baig and Mohammad I. Admani, PO Box 590, El Centro, CA 92243.

FAMILY PRACTITIONER needed for multispecialty group of 27 physicians in town of 25,000 in agricultural area 20 miles from state capitol. Clinic adjacent to 150-bed hospital. $70,000 guarantee plus bonus first year. Full stockholder status thereafter plus many fringe benefits. Close to excellent outdoor recreational activities. Contact Mike Crane, 215 E. Hawaii, Nampa, ID 83651; (208) 467-1121.

BEAUTIFUL MONTEREY BAY. Immediate opportunity for a friendly, skilled, Family Practice or Emergency Physician to join highly respected urgent care group with two beautiful Santa Cruz clinics. Committed to high quality care. Nice people, flexible scheduling, comprehensive benefits, including: paid malpractice, group health insurance, long-term disability insurance, no nights, rapid advancement to full partnership in an outstanding place to live. Please send CV to Robert Korns, MD, 6800 Soquel Dr, Aptos, CA 95003 or call (408) 662-3611.

PHYSICIANS WANTED

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Excellent compensation and benefits including free housing, school tuition for children and major tax savings for one year and over appointments. Minimum of three years professional experience required.

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MEDICAL COORDINATOR FOR LIVER TRANSPLANTATION. The University of California in San Francisco is recruiting for an Assistant or Associate Professor of Clinical Medicine responsible for coordinating medical aspects of liver transplantation program including: preoperative evaluation of prospective recipients; liaison with other medical specialties and supporting services; medical aspects of postoperative care. Candidates should be at least one year beyond completion of training in Gastroenterology, certified by the Board of Internal Medicine in both Medicine and Gastroenterology, provide tangible evidence of clinical, teaching and research accomplishment, and demonstrate personal characteristics necessary for effective interaction in a multidisciplinary environment. Rank and salary will be commensurate with qualifications. Interested individuals should reply to Robert K. Ockner, MD, Division of Gastroenterology, Box 0538, University of California, San Francisco, CA 94143. UCSF is an Equal Opportunity/Affirmative Action employer. Women and minorities are encouraged to apply.

WESTERN MONTANA FAMILY PRACTICE. Family Practitioner seeks associate for busy office practice. Small town near regional hospitals. Surgery assists, no OB. Excellent climate, recreation, and schools. Résumé and inquiries to Number 95, Western Journal of Medicine, PO Box 7602, San Francisco, CA 94120-7602.

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(Continued on Page 381)

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1 Sontag S, Robinson M, McCallum R, et al. Ranitidine therapy for gastroesophageal reflux disease: Results of a large double-blind trial. *Arch Intern Med* 1987; 147:1485-1491.

See next page for Brief Summary of Product Information

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(Continued from Page 376)

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(Continued on Page 384)

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(Continued from Page 381)

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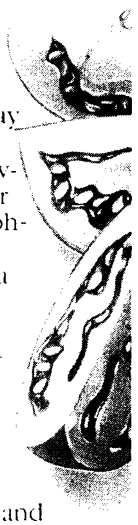
A defense against cancer can be cooked up in your kitchen.



There is evidence that diet and cancer are related. Some foods may promote cancer, while others may protect you from it.

Foods related to lowering the risk of cancer of the larynx and esophagus all have high amounts of carotene, a form of Vitamin A which is in cantaloupes, peaches, broccoli, spinach, all dark green leafy vegetables, sweet potatoes, carrots, pumpkin, winter squash, and tomatoes, citrus fruits and brussels sprouts.

Foods that may help reduce the risk of gastrointestinal and respiratory tract cancer are cabbage, broccoli, brussels sprouts, kohlrabi, cauliflower.

Fruits, vegetables and whole-grain cereals such as oatmeal, bran and wheat may help lower the risk of colorectal cancer.

Foods high in fats, salt- or nitrite-cured foods such as ham, and fish and types of sausages smoked by traditional methods should be eaten in moderation.

Be moderate in consumption of alcohol also.

A good rule of thumb is cut down on fat and don't be fat. Weight reduction may lower cancer risk. Our 12-year study of nearly a million Americans uncovered high cancer risks particularly among people 40% or more overweight.

Now, more than ever, we know you can cook up your own defense against cancer. So eat healthy and be healthy.

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AMERICAN CANCER SOCIETY

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ceftriaxone sodium/Roche

Before prescribing, please consult complete product information, a summary of which follows:

INDICATIONS AND USAGE: Rocephin is indicated for the treatment of the following infections when caused by susceptible organisms.

LOWER RESPIRATORY TRACT INFECTIONS caused by *Strep. pneumoniae, Streptococcus* species (excluding enterococci), *Staph. aureus, H. influenzae, H. parainfluenzae, Klebsiella* species (including *K. pneumoniae*), *E. coli, E. aerogenes, Proteus mirabilis* and *Serratia marcescens*.

SKIN AND SKIN STRUCTURE INFECTIONS caused by *Staph. aureus, Staph. epidermidis, Streptococcus* species (excluding enterococci), *E. cloacae, Klebsiella* species (including *K. pneumoniae*), *Proteus mirabilis* and *Pseudomonas aeruginosa*.

URINARY TRACT INFECTIONS (complicated and uncomplicated) caused by *E. coli, Proteus mirabilis, Proteus vulgaris, M. morganii* and *Klebsiella* species (including *K. pneumoniae*).

UNCOMPLICATED GONORRHEA (cervical/urethral and rectal) caused by *Neisseria gonorrhoeae*, including both penicillinase and nonpenicillinase producing strains.

PELVIC INFLAMMATORY DISEASE caused by *N. gonorrhoeae*.

BACTERIAL SEPTICEMIA caused by *Staph. aureus, Strep. pneumoniae, E. coli, H. influenzae* and *K. pneumoniae*.

BONE AND JOINT INFECTIONS caused by *Staph. aureus, Strep. pneumoniae, Streptococcus* species (excluding enterococci), *E. coli, P. mirabilis, K. pneumoniae* and *Enterobacter* species.

INTRA-ABDOMINAL INFECTIONS caused by *E. coli* and *K. pneumoniae*.

MENINGITIS caused by *H. influenzae, N. meningitidis* and *Strep. pneumoniae*. Ceftriaxone has also been used successfully in a limited number of cases of meningitis and shunt infections caused by *Staph. epidermidis* and *E. coli*.

SURGICAL PROPHYLAXIS. Preoperative administration of a single 1 gm dose may reduce incidence of postoperative infections in patients undergoing surgical procedures classified as contaminated or potentially contaminated (*e.g.*, vaginal or abdominal hysterectomy) and in those for whom infection at the operative site presents serious risk (*e.g.*, during coronary artery bypass surgery).

Although ceftriaxone has been shown to have been as effective as cefazolin in the prevention of infection following coronary artery bypass surgery, no placebo-controlled trials have been conducted to evaluate any cephalosporin antibiotic in the prevention of infection following coronary artery bypass surgery. When administered before indicated surgical procedures, a single 1 gm dose provides protection from most infections due to susceptible organisms for duration of procedure.

SUSCEPTIBILITY TESTING. Before instituting treatment with Rocephin, appropriate specimens should be obtained for isolation of the causative organism and for determination of its susceptibility to the drug. Therapy may be instituted prior to obtaining results of susceptibility testing.

CONTRAINDICATIONS: Rocephin is contraindicated in patients with known allergy to the cephalosporin class of antibiotics.

WARNINGS: BEFORE THERAPY WITH ROCEPHIN IS INSTITUTED, CAREFUL INQUIRY SHOULD BE MADE TO DETERMINE WHETHER THE PATIENT HAS HAD PREVIOUS HYPERSENSITIVITY REACTIONS TO CEPHALOSPORINS, PENICILLINS OR OTHER DRUGS. THIS PRODUCT SHOULD BE GIVEN CAUTIOUSLY TO PENICILLIN-SENSITIVE PATIENTS. ANTIBIOTICS SHOULD BE ADMINISTERED WITH CAUTION TO ANY PATIENT WHO HAS DEMONSTRATED SOME FORM OF ALLERGY, PARTICULARLY TO DRUGS. SERIOUS ACUTE HYPERSENSITIVITY REACTIONS MAY REQUIRE THE USE OF SUBCUTANEOUS EPINEPHRINE AND OTHER EMERGENCY MEASURES.

Pseudomembranous colitis has been reported with the use of cephalosporins (and other broad-spectrum antibiotics), therefore, it is important to consider its diagnosis in patients who develop diarrhea in association with antibiotic use.

Treatment with broad-spectrum antibiotics alters the normal flora of the colon and may permit overgrowth of clostridia. Studies indicate a toxin produced by *Clostridium difficile* is one primary cause of antibiotic-associated colitis. Cholestyramine and colestipol resins have been shown to bind to the toxin *in vitro*.

Mild cases of colitis respond to drug discontinuance alone. Moderate to severe cases should be managed with fluid, electrolyte and protein supplementation as indicated.

When the colitis is not relieved by drug discontinuance or when it is severe, oral vancomycin is the treatment of choice for antibiotic-associated pseudomembranous colitis produced by *C. difficile*. Other causes of colitis should also be considered.

Rarely, shadows suggesting sludge have been detected by sonograms of the gallbladder in asymptomatic and symptomatic patients. This appears to be reversible on discontinuation of therapy. In a few symptomatic patients receiving higher than usual doses, who underwent surgery, sludge containing traces of ceftriaxone was recovered from surgical specimens. Discontinue therapy in patients who develop signs or symptoms suggestive of gallbladder disease; consider conservative management.

PRECAUTIONS: *GENERAL*. Although transient elevations of BUN and serum creatinine have been observed, at the recommended dosages, the nephrotoxic potential of Rocephin is similar to that of other cephalosporins.

Ceftriaxone is excreted via both biliary and renal excretion (see Clinical Pharmacology). Therefore, patients with renal failure normally require no adjustment in dosage when usual doses of Rocephin are administered, but concentrations of drug in the serum should be monitored periodically. If evidence of accumulation exists, dosage should be decreased accordingly.

Dosage adjustments should not be necessary in patients with hepatic dysfunction, however, in patients with both hepatic dysfunction and significant renal disease, Rocephin dosage should not exceed 2 gm daily without close monitoring of serum concentrations.

Alterations in prothrombin times have occurred rarely in patients treated with Rocephin. Patients with impaired vitamin K synthesis or low vitamin K stores (*e.g.*, chronic hepatic disease and malnutrition) may require monitoring of prothrombin time during Rocephin treatment. Vitamin K administration (10 mg weekly) may be necessary if the prothrombin time is prolonged before or during therapy.

Prolonged use of Rocephin may result in overgrowth of nonsusceptible organisms. Careful observation of the patient is essential. If superinfection occurs during therapy, appropriate measures should be taken.

Rocephin should be prescribed with caution in individuals with a history of gastrointestinal disease, especially colitis.

CARCINOGENESIS, MUTAGENESIS, IMPAIRMENT OF FERTILITY. Carcinogenesis. Considering the maximum duration of treatment and the class of the compound, carcinogenicity studies with ceftriaxone in animals have not been performed. The maximum

duration of animal toxicity studies was six months.

Mutagenesis. Genetic toxicology tests included the Ames test, a micronucleus test and a test for chromosomal aberrations in human lymphocytes cultured *in vitro* with ceftriaxone. Ceftriaxone showed no potential for mutagenic activity in these studies.

Impairment of Fertility. Ceftriaxone produced no impairment of fertility when given intravenously to rats at daily doses up to 586 mg/kg/day, approximately 20 times the recommended clinical dose of 2 gm/day.

PREGNANCY. Teratogenic Effects. Pregnancy Category B. Reproductive studies have been performed in mice and rats at doses up to 20 times the usual human dose and have no evidence of embryotoxicity, fetotoxicity or teratogenicity. In primates, no embryotoxicity or teratogenicity was demonstrated at a dose approximately three times the human dose.

There are, however, no adequate and well-controlled studies in pregnant women. Because animal reproductive studies are not always predictive of human response, this drug should be used during pregnancy only if clearly needed.

Nonteratogenic Effects. In rats, in the Segment I (fertility and general reproduction) and Segment III (perinatal and postnatal) studies with intravenously administered ceftriaxone, no adverse effects were noted on various reproductive parameters during gestation and lactation, including postnatal growth, functional behavior and reproductive ability of the offspring, at doses of 586 mg/kg/day or less.

NURSING MOTHERS. Low concentrations of ceftriaxone are excreted in human milk. Caution should be exercised when Rocephin is administered to a nursing woman.

PEDIATRIC USE. Safety and effectiveness of Rocephin in neonates, infants and children have been established for the dosages described in the Dosage and Administration section. *In vitro* studies have shown ceftriaxone, like some other cephalosporins, can displace bilirubin from serum albumin. Exercise caution before administration to hyperbilirubinemic neonates, especially prematures.

ADVERSE REACTIONS: Rocephin is generally well tolerated. In clinical trials, the following adverse reactions, which were considered to be related to Rocephin therapy or of uncertain etiology, were observed:

LOCAL REACTIONS— pain, induration or tenderness at the site of injection (1%). Less frequently reported (less than 1%) was phlebitis after I.V. administration.

HYPERSENSITIVITY— rash (1.7%). Less frequently reported (less than 1%) were pruritus, fever or chills.

HEMATOLOGIC— eosinophilia (6%), thrombocytosis (5.1%) and leukopenia (2.1%). Less frequently reported (less than 1%) were anemia, neutropenia, lymphopenia, thrombocytopenia and prolongation of the prothrombin time.

GASTROINTESTINAL— diarrhea (2.7%). Less frequently reported (less than 1%) were nausea or vomiting, and dysgeusia.

HEPATIC— elevations of SGOT (3.1%) or SGPT (3.3%). Less frequently reported (less than 1%) were elevations of alkaline phosphatase and bilirubin.

RENAL— elevations of the BUN (1.2%). Less frequently reported (less than 1%) were elevations of creatinine and the presence of casts in the urine.

CENTRAL NERVOUS SYSTEM— headache or dizziness were reported occasionally (less than 1%).

GENITOURINARY— moniliasis or vaginitis were reported occasionally (less than 1%).

MISCELLANEOUS— diaphoresis and flushing were reported occasionally (less than 1%).

Other rarely observed adverse reactions (less than 0.1%) include leukocytosis, lymphocytosis, monocytosis, basophilia, a decrease in the prothrombin time, jaundice, gallbladder sludge, glycosuria, hematuria, anaphylaxis, bronchospasm, serum sickness, abdominal pain, colitis, flatulence, dyspepsia, palpitations and epistaxis.

DOSAGE AND ADMINISTRATION: Rocephin may be administered intravenously or intramuscularly. The usual adult daily dose is 1 to 2 gm given once a day (or in equally divided doses twice a day) depending on the type and severity of the infection. The total daily dose should not exceed 4 grams.

For the treatment of serious miscellaneous infections in children, other than meningitis, the recommended total daily dose is 50 to 75 mg/kg (not to exceed 2 grams), given in divided doses every 12 hours.

Generally, Rocephin therapy should be continued for at least two days after the signs and symptoms of infection have disappeared. The usual duration is 4 to 14 days; in complicated infections longer therapy may be required.

In the treatment of meningitis, a daily dose of 100 mg/kg (not to exceed 4 grams), given in divided doses every 12 hours, should be administered with or without a loading dose of 75 mg/kg.

For the treatment of uncomplicated gonococcal infections, a single intramuscular dose of 250 mg is recommended.

For preoperative use (surgical prophylaxis), a single dose of 1 gm administered 1/2 to 2 hours before surgery is recommended.

When treating infections caused by *Streptococcus pyogenes*, therapy should be continued for at least ten days.

No dosage adjustment is necessary for patients with impairment of renal or hepatic function; however, blood levels should be monitored in patients with severe renal impairment (*e.g.*, dialysis patients) and in patients with both renal and hepatic dysfunctions.

HOW SUPPLIED: Rocephin (ceftriaxone sodium/Roche) is supplied as a sterile crystalline powder in glass vials and piggyback bottles. The following packages are available:

Vials containing 250 mg, 500 mg, 1 gm or 2 gm equivalent of ceftriaxone, piggyback bottles containing 1 gm or 2 gm equivalent of ceftriaxone, bulk pharmacy containers containing 10 gm equivalent of ceftriaxone (NOT FOR DIRECT ADMINISTRATION).

Also supplied as a sterile crystalline powder as follows:
ADD-Vantage Vials** containing 1 gm or 2 gm equivalent of ceftriaxone.

Also supplied premixed as a frozen iso-osmotic, sterile, nonpyrogenic solution of ceftriaxone sodium in 50 mL single dose plastic containers,† as follows:

1 gm equivalent of ceftriaxone, iso-osmotic with approximately 1.9 gm dextrose hydrous, USP added.

2 gm equivalent of ceftriaxone, iso-osmotic with approximately 1.2 gm dextrose hydrous, USP added.

NOTE: Rocephin in the frozen state should not be stored above -20°C.

*Registered trademark of Abbott Laboratories, Inc.

†Manufactured for Roche Laboratories, Division of Hoffmann-La Roche Inc., by Travenol Laboratories, Inc., Deerfield, Illinois 60015.

P.I. 0587

Roche Laboratories
a division of Hoffmann-La Roche Inc.

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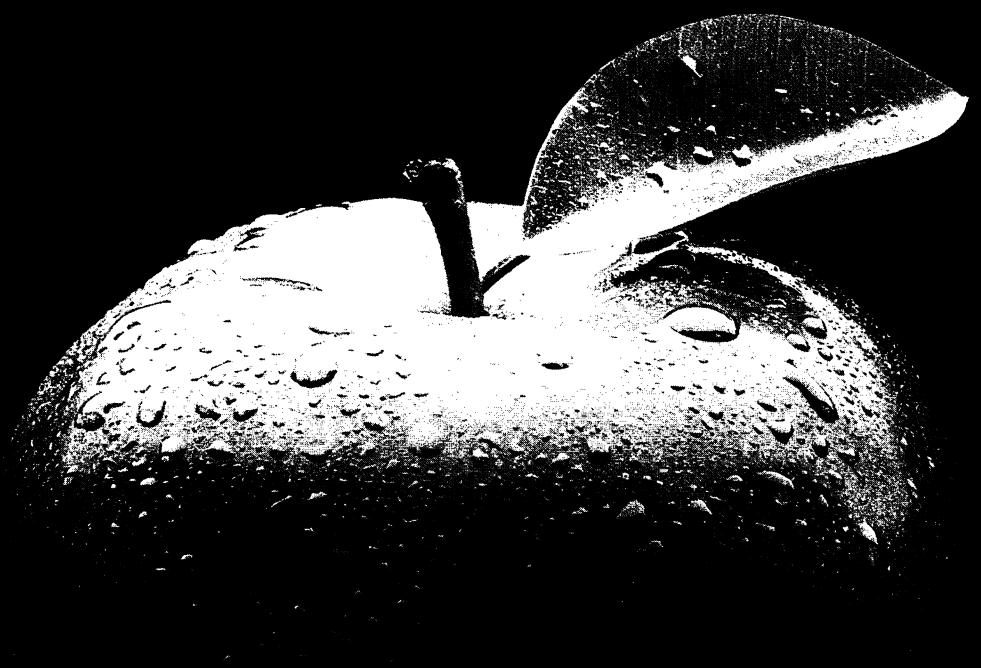

Once-a-day

Rocephin® IV·IM

ceftriaxone sodium/Roche

Please see adjacent page for summary of product information.

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